A STUDY OF INFLUENCE OF DURATION OF UNTREATED PSYCHOSIS ON THE SHORT TERM OUTCOME IN FIRST EPISODE SCHIZOPHRENIA IN INSTITUTE OF MENTAL HEALTH, MADRAS MEDICAL COLLEGE, CHENNAI

Dissertation submitted to

THE TAMIL NADU DR. M. G. R. MEDICAL UNIVERSITY

in part fulfillment of the requirements for

DOCTOR OF MEDICINE

(BRANCH – XVIII) PSYCHIATRY

EXAMINATIONS - APRIL 2015

INSTITUTE OF MENTAL HEALTH,

MADRAS MEDICAL COLLEGE, CHENNAI 10.

April 2015

CERTIFICATE

This is to certify that this dissertation titled "**A STUDY OF INFLUENCE OF DURATION OF UNTREATED PSYCHOSIS ON THE SHORT TERM OUTCOME IN FIRST EPISODE SCHIZOPHRENIA IN INSTITUTE OF MENTAL HEALTH"** submitted by **DR. K. BHARATHI**, appearing for **M.D (Psychiatry)** degree examination in April 2015 is a original bonafide record of work done her under my guidance and supervision in part fulfillment of requirements of the Tamil Nadu Dr. M.G.R. Medical University, Chennai. I forward this to the Tamil Nadu Dr. M.G.R. Medical University, Chennai, Tamil Nadu, India.

The Director,
Institute of Mental Health,
Chennai – 10.

The Dean,
Madras Medical College,
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CERTIFICATE OF GUIDE

This is to certify that the dissertation titled, **"A STUDY OF INFLUENCE OF DURATION OF UNTREATED PSYCHOSIS ON THE SHORT TERM OUTCOME IN FIRST EPISODE SCHIZOPHRENIA IN INSTITUTE OF MENTAL HEALTH"** is the original work of **Dr. K. BHARATHI**, done under my guidance submitted in partial fulfilment of the requirements for M.D. Branch – XVIII [Psychiatry] examination of The Tamilnadu Dr. M. G. R. Medical University, to be held in April 2015.

DR. W.J. ALEXANDARGNANADURAI,
Associate Professor,
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Chennai

DECLARATION

I, Dr. K.BHARATHI, solemnly declare that this dissertation **"A STUDY OF INFLUENCE OF DURATION OF UNTREATED PSYCHOSIS ON THE SHORT TERM OUTCOME IN FIRST EPISODE SCHIZOPHRENIA IN INSTITUTE OF MENTAL HEALTH, MADRAS MEDICAL COLLEGE, CHENNAI"** was done by me at Institute of Mental Health, Madras Medical College, Chennai under my guidance and supervision of the Professor of Psychiatry, Madras Medical College, Chennai.

This dissertation is submitted to the Tamil Nadu Dr.M.G.R. Medical University, Chennai – 32 in partial fulfilment of the University requirements for the award of the degree of M.D., Psychiatry.

DR. K. BHARATHI

Place : Chennai

Date : 29.09.2014

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INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

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CERTIFICATE OF APPROVAL

To
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Postgraduate MD(Psychiatry),
Madras Medical College,
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Dear Dr. K. Bharathi,

The Institutional Ethics Committee has considered your request and approved your study titled **"Influence of duration of untreated psychosis on the short term outcome in first episode schizophrenia " No.22082014.**

The following members of Ethics Committee were present in the meeting held on 05.08.2014 conducted at Madras Medical College, Chennai-3.

1.	Dr.C.Rajendran, M.D.,	: Chairperson
2.	Dr.R.Vimala, M.D., Dean, MMC, Ch-3	: Deputy Chairperson
3.	Prof.B.Kalaiselvi, M.D., Vice-Principal, MMC, Ch-3	: Member Secretary
4.	Prof.R.Nandhini, M.D., Inst.of Pharmacology, MMC	: Member
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10.	Thiru S.Govindasamy, B.A., B.L.,	: Lawyer
11.	Tmt.Arnold Saulina, M.A., MSW.,	: Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
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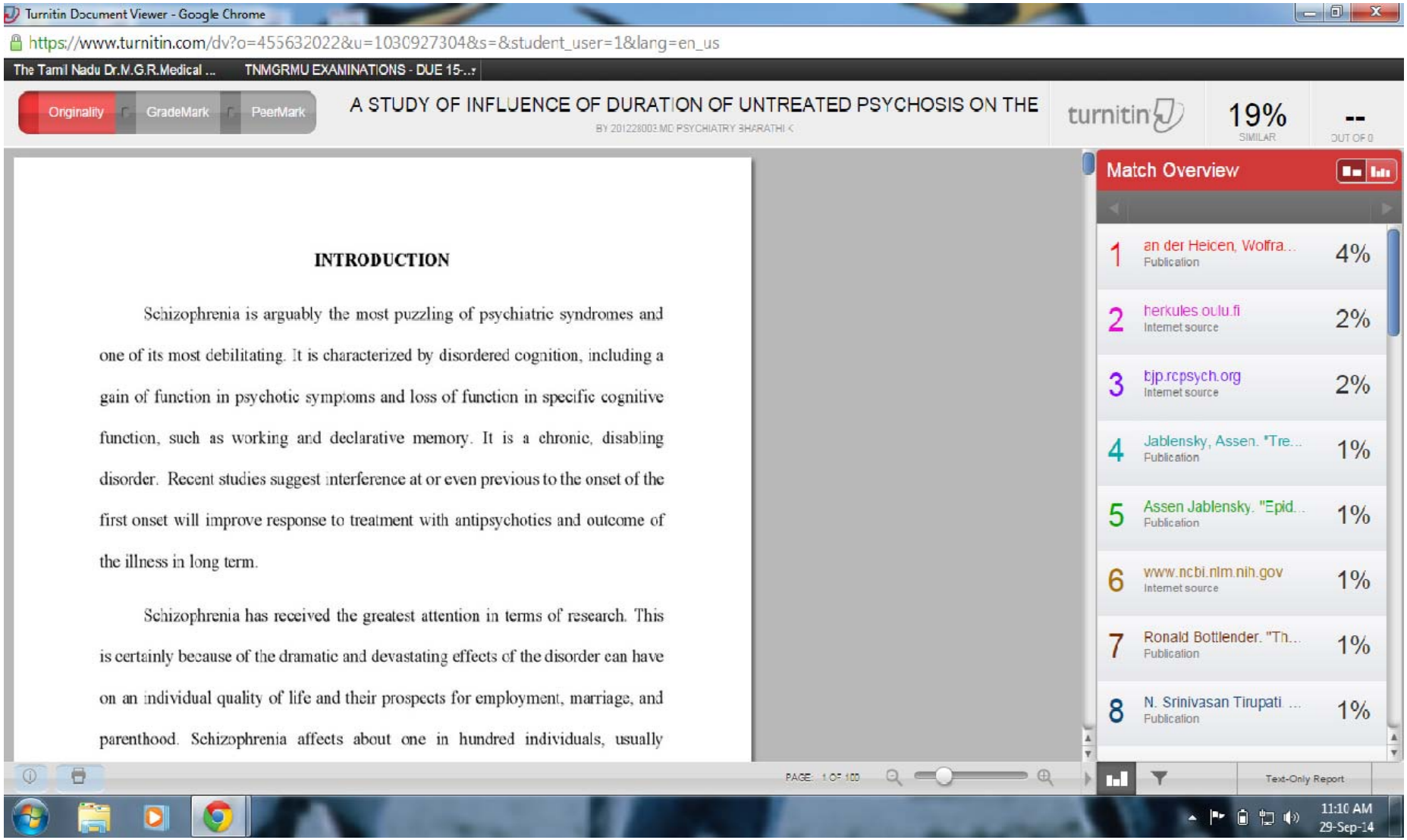
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INTRODUCTION
Schizophrenia is arguably the most puzzling of psychiatric syndromes and one of its most debilitating. It is characterized by disordered cognition, including a gain of function in psychotic symptoms and loss of function in specific cognitive function, such as working and declarative memory. It is a chronic, disabling disorder. Recent studies suggest interference at or even previous to the onset of the first onset will improve response to treatment with antipsychotics and outcome of the illness in long term.
Schizophrenia has received the greatest attention in terms of research. This is certainly because of the dramatic and devastating effects of the disorder can have on an individual quality of life and their prospects for employment, marriage, and parenthood. Schizophrenia affects about one in hundred individuals, usually
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ABSTRACT

Objective: Previous studies have suggested that there may be an association between longer duration of untreated psychosis and poor outcome in first episode schizophrenia. These studies have been interpreted as providing evidence that untreated psychosis may constitute an active morbid process that is “toxic” to the brain. If untreated psychosis is neurotoxic, this would form a strong basis for early intervention in schizophrenia.

Method: Fifty seven neuroleptic-naïve patients with ICD-10 schizophrenia were evaluated 12 weeks after their first inpatient hospitalization. We examined the relationship between untreated initial psychosis duration (measured from onset of first symptom as well as from first hospital admission) by conducting clinical interview, symptom severity by PANSS and CGI-S scale, premorbid social adjustment by PSA scale, and symptoms improvement after treatment by CGI-I scale.

Results: Earlier age at illness onset was associated with longer duration of untreated prodromal psychotic symptoms. There were no significant gender

differences in duration of untreated initial psychosis. There is significant association between untreated psychosis duration and premorbid functioning. After controlling for the effects of age at onset, the duration of untreated initial psychosis did not significantly impair subsequent symptom severity or remission of positive symptoms.

Conclusions: Significant negative correlation between duration of untreated psychosis and the age at first presentation and positive symptoms at the time of onset of psychosis. Significant positive correlation between the duration of untreated psychosis and premorbid adjustment. This finding concludes that after controlling of all the confounding factors the duration of untreated psychosis is an independent predictor of outcome as stated in literature. So, early intervention is necessary.

Key words: first-episode schizophrenia, premorbid adjustment, follow up, duration of untreated psychosis (DUP), clinical outcome.

INTRODUCTION

Schizophrenia is arguably the most puzzling of psychiatric syndromes and one of its most debilitating. It is characterized by disordered cognition, including a gain of function in psychotic symptoms and loss of function in specific cognitive function, such as working and declarative memory. It is a chronic, disabling disorder. Recent studies suggest interference at or even previous to the onset of the first onset will improve response to treatment with antipsychotics and outcome of the illness in long term.

Schizophrenia has received the greatest attention in terms of research. This is certainly because of the dramatic and devastating effects of the disorder can have on an individual quality of life and their prospects for employment, marriage, and parenthood. Schizophrenia affects about one in hundred individuals, usually beginning in late adolescent or early adulthood. Untreated, it runs a chronic, deteriorating course. In addition to the personal tragedy schizophrenia creates a substantial public health burden due to the cost of lifelong health care needs and lost productivity.

There are effective interventions that can benefit individuals and help them to lead a more normal life.

Current research is directed towards establishing the causes of schizophrenia and investigating possibility of early interventions in those identified at high risk for the disorder or with prodromal symptoms.

Research has consistently shown that longer duration of untreated psychosis is associated with poorer outcomes among persons with schizophrenia.

Meta-analysis of studies suggested that delay in the initiation of treatment for psychosis and an increased level of duration of untreated psychosis is related with a poorer response to treatment and outcome in countries like India.

Schizophrenia may be “biologically toxic” as suggested by Wyatt and that long-term morbidity due to psychosis may be prevented if patients were treated by anti-psychotics as early as possible.

Duration of Untreated Psychosis (DUP) has been reported as a self-determining marker of prognostic outcome; measurement error and variability in DUP in terms of heterogenecity have also been reported. Only moderately strong association was observed between DUP and Outcome, based on presented data 13% of variant are one third to one fourth who did not achieve remission.

First episode of schizophrenia:

Many people experiencing their first episode will have no personal or family experience of mental ill health and some will lack insight that symptoms or a result of mental illness. As a result many patients will present in crisis and not directly complaining of psychotic symptoms.

The range possible presentation is very wide.

Commonly seen are

1. Spouse or relative noticing withdrawn or bizarre behavior
2. Failure to achieve educational potential with referral by school or student health services.
3. Onset of personality change, social withdrawal, odd behavior.
4. Presentation via criminal justice system.
5. Presentation following deliberate self harm or suicidal attempt.
6. First sign may be symptoms of other disorder (Depression, Mania, OCD, Panic disorder)

First episode schizophrenia is often time diagnostic, may take month/year. It is usually necessary to admit people suspected of first schizophrenic episode in order to assess the extent of their psychopathology to provide, time for education and pharmacological and psychological treatment.

Drake *et al* observed a significant relationship between the DUP and prognosis of short term illness: earlier is the treatment, the better is

the improvement. This is due to the factors that impede the period between having a psychotic symptom and seeking treatment for it are the same ones that prevent effective treatment response. So, evaluating the reasons for delayed treatment is valuable.

Symptoms of psychosis are alarming for the person and for his family and his friends. Degree of symptoms interrupts education, work, and interpersonal relationships. If these symptoms are allowed to continue unchanged, they potentially deteriorate self confidence, friendships, family relation, and educational and vocational success.

REVIEW OF LITERATURE

Emil Kraeplin (1856 to 1926) first delineated dementia praecox. Eugene Bleuler (1857 to 1959) coined the term Schizophrenia. He proposed the name denote a splitting of psychic functions which he considered to the basis of the illness. His description of the illness include 4 primary symptoms were abnormal association, autistic behavior and thinking, abnormal affect and ambivalence.

Bleuler considered the loss of association between thought process and thought, emotion, and behavior to be the hallmark of the illness. Hallucination, delusion, and social withdrawal diminished drive as secondary manifestation of the illness. He saw symptoms of schizophrenia in a continuum with normal behavior. He was less concerned with the course of the illness.

Kraeplin much more concerned with the understanding of the psychological mechanism underlying the disease process. He identified that schizophrenia rested on course and outcome. He also found that the recovery from schizophrenia was very rare, or even impossible, deteriorating and irreversible. He believed that dementia praecox was loss of the inner unity of the activities of intellect, emotion and volition. His appraisal of the outcome has been challenged by subsequent follow-up studies.

Kurt Schneider (1887 to 1967) in his classification of thought disorders attempted to make the diagnosis of schizophrenia more reliable by identifying a group of symptoms of schizophrenia that were the most characteristic of the illness. His so called first rank symptoms included various forms of hallucinations, thought withdrawal, thought insertion, thought broadcasting, delusional perceptions and experiencing feelings and actions as made or influenced by external agents. The presence of one of the symptoms, in the absence of intoxication, brain injury or clear affective illness, was taken as sufficient for making the diagnosis of schizophrenia.

Psychotic symptoms (Positive symptoms):

1. Hallucination
2. Delusion

Psychotic symptoms of schizophrenia define schizophrenia for the general public and for most physicians. They are the most obvious and dramatic symptoms of the illness, and for most people they are what is fascinating and frightening about schizophrenia. IPSS studies suggest that more than 70% of people with schizophrenia have auditory hallucinations, and that percentage is probably higher in industrialized societies. The most common theme found in schizophrenia is persecutory;

it might be that the most common inciting event for the formation of a delusion is need to explain experience of auditory hallucination.

The validity of the hallucinatory experiences seems self evident to most patients. Potentially less distressing themes, like grandiose and religious content in delusions, are experienced by half or fewer people with schizophrenia. It can be generally expected that delusion of persecution or religious content will have the most effect on patients behavior, although the response of each patients to each thought is of course dependent on that person and that situation.

A review of investigation into the nature of the delusion finds that fact there does appear to be a root to delusion that can be understood outside the idiosyncratic experiences of the patient who experiences a "direct experience of meaning".

Negatives symptoms:

1. Restricted affect,
2. Diminished emotional range,
3. Poverty of speech,
4. Curbing of interest,
5. Diminished sense of purpose,
6. Diminished social drive.

Severity of Negative symptoms predicts long term disability better than the severity of psychotic or disorganization symptoms. Positive and negative syndrome concept as formulated by T.J.Crow. Most people with schizophrenia will experience depression and anxiety during their course of illness, depression has been variably reported as good prognostic feature and as a poor prognostic feature, it seems likely that depression in schizophrenia caries the same burdens it does for the other people and so adds to the burden of the illness, but the presence of significant depression might also be an indirect indicator of absence of the deficit syndrome and the long term disability associated with primary negative symptoms.

Disorganisation:

Disorganisation syndrome has been part of the conception of the schizophrenia. Since Kreaplin included hebephrenia in dementia prarcox but the behaviors experiences and associated pathology have been subject to less investigation than the psychotic and negative symptoms. Disorganisation symptoms certainly include,

1. The formal thought disorder
2. Bizarre and catatonic behavior
3. Inappropriate affect

Disorganisation can also include agitation and aggression including assuming postures, suggesting the person is preparing for violence, swearing, or broad movements of arms are the trunk as the patient ambulance. Hygiene is frequently poor and as a group those with disorganized schizophrenia or more indifferent to routine activities of daily living or health care and healthcare maintenance, than are other patients with schizophrenia.

Motor symptoms:

Motor behavior can include subtle repetitive hand movements or broad, complex and purposeless movements involve limbs and trunk, mannerisms, echopraxia, tics and symptoms of catatonia.

Pathophysiology of Schizophrenia:

There is neither is single brain region nor a single neurochemical alteration, but several, which have been associated with schizophrenia. The prefrontal cortex, hippocampus, and thalamus are the regions most often implicated. At cellular level reduced gray matter volumes, reduced size of neurons but without cell loss and reduced dentritic arborization and spines are the main observations seen in schizophrenia. The cause remains unknown, but the implication of the finding is one of reduced connectivity in brain. Neurochemical deficits in neurotransmitter system indicate abnormal synaptic communications between neurons. The

evidence suggests that deficit in the GABAnergic system in the neocortical regions and Glutamate system in the hippocampus exist, but it is premature to state this with certainty. However, neurochemical abnormalities would certainly be expected impair neuronal communication. White matter may also contribute to connectivity deficits between brain regions implicated in schizophrenia. Taken together, schizophrenia is disease of abnormal connectivity, one that may occur at cellular level, synaptic level or circuit level. These findings have lead to speculation that frontal-temporal/parietal connectivity may be the final common pathway for the development of schizophrenia.

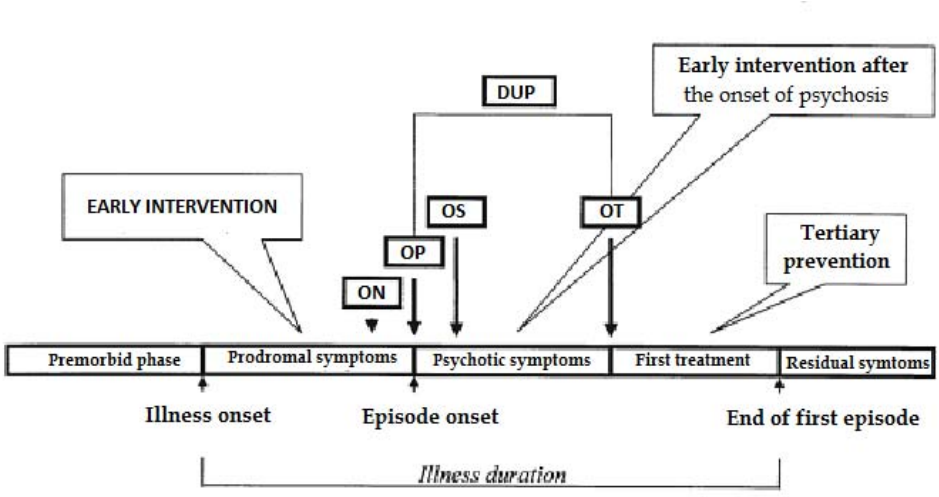
Researchers have focused on finding the single protein that would explain schizophrenia. A shift in conceptual framework from searching for a specific protein defect (key protein targets dysregulated in brain substrates) in schizophrenia to searching for defects in neural networks underlying symptom domains may represent a plausible approach to investigating the pathophysiology of schizophrenia.

A number of other theories exist including those which postulate that schizophrenia is a neurodegenerative disorder, abnormality of information processing, meta-representation/theory of mind, working memory, neuronal migration or language.

Duration of untreated psychosis:

Duration of untreated psychosis (DUP) is defined as delay in treatment with antipsychotics which was found to be associated with an unfavourable outcome of schizophrenia.

Starting treatment as early in new onset of psychosis is a major concern worldwide. Many services are being recognized to provide and to support earlier detection and treatment of new onset of schizophrenia and other psychoses.



ON - Onset of Negative symptoms
OP - Onset of Positive symptoms
OS - Onset of Syndrome
OT - Onset of Treatment
DUP - Duration of Untreated Psychosis

Fig. 1: Duration of untreated psychosis is period between the onset of positive symptoms and starting of first treatment. End of first episode is at the end of first treatment.

Premorbid phase: This is the first phase which is normal period for most of the patients, who eventually develop schizophrenia, when deficit be present they are usually slight, stable and symptomless.

Prodromal Phase: It is the second phase which begins after puberty where symptoms develop with rising severity and downhill decline of global functioning.

This period lasts two to five years in average.

Pschotic phase: It is the third phase with profound psychotic symptoms in this period patient feels convinced that his hallucinations and delusions are true with the absence of insight in initial phase of the illness.

Variations in the course and outcome of schizophrenia:

Systematic investigations into the course and outcome of schizophrenia where initiated by Kreaplin, who believed that the natural history of the disorder could provide a provisional validation of the disease concept, until final verification could be achieved by brain pathology. Contrary to Kreaplin postulate of mental weakness is precisely the long term course of schizophrenia that reveals the greatest extent of variation across population and culture. The course and outcome of schizophrenia exhibit striking heterogenicity and variability, both across and within population. Patient with similar clinical and

diagnostic characteristic of baseline assessment develop a broad spectrum of outcome ranging from stable, clinical and social recovery after a single psychotic episode to chronic unremitting psychosis and severe impairment.

Long term follow up studies lend creditability to the conclusion that high proportion (30 %) of patients meeting the diagnostic criteria for schizophrenia may achieve relatively favorable outcome.

Secular trends in outcome of schizophrenia:

A long term prospective on the course of schizophrenia over the successive generations is provided by a meta analysis of 320 outcome studies on schizophrenia or dementia praecox published between 1895 and 1992 which comprise 51,800 subjects, overall 40% of the patients have been described as improved after an average length of follow up 5.6 years. There was a significant increase in the rate of improvement during 1956 to 1985 compared to 1895 to 1955, clearly related to introduction of neuroleptic treatment but a secular trend toward better outcome with every successive decade has been present for much longer. Coupled with virtual disappearance of the most malignant or catastrophic forms of schizophrenia which tendered to result in a profound defect state after a single psychotic episode or in death (lethal catatonia), these observation suggests that a transition to a less deteriorating course of schizophrenia

had been taking place prior to the advent of modern pharmacological treatment.

Concurrently with above trends in Europe and North America, reports from developing countries, usually based on small clinical samples pointed to a less disabling course and a high rate of recovery from schizophrenic psychosis in traditional societies Mauritus and Sri Lanka. Good outcome cases included who would be expected to the poor outcome if Western prognostic criteria have been applied, however selection bias could not be excluded, as these studies were based on hospital admission only.

In addition, clinical improvement could have been confounded with social adjustment many patients achieve in a comparatively undemanding environment.

Many methods for an early recognition of psychosis risk were developed and their strength was experienced in the last two decades. They allow us to assess psychotic prodromal symptoms and pre-psychotic signs, and to foretell conversion to psychosis with different probabilities as suggested by Hafner and Maurer, 2006; Miller et al., 1999; and Yung in 2006.

Commonly measured outcomes in schizophrenia are positive and negative symptom outcomes, cognitive function outcome,

neurobiological function outcomes, patient reported outcome, wider societal outcome, duration of untreated psychosis outcomes, and economic outcomes.

The prolonged course of schizophrenia foregoing the first treatment contact has provoked the question whether the DUP or duration of untreated illness (DUI) is a predictor of a poor outcome. Results from studies on association with various indicators of a poor outcome – symptoms, cognitive deficits, social decline and frequency of relapses – are not completely reliable. The reason is not having a standardized study group composition and description and dimension of the onset of DUP and DUI.

In 1996 McGlashan and Johannessen, presumed that deficits may be due to an attenuated synaptic plasticity of brain. The disease becomes chronic, if the fundamental disease process of psychosis is not treated with antipsychotic medicines. So, the antipsychotic treatment is having a benign effect on the underlying disease process or facilitates to conserve the plasticity of the brain.

The association between DUP has been established by many studies, mostly defined by the first episode of persistent psychotic symptoms, and indicators of the course of the first episode or one year outcome using mainly clinical interviews. Darke et al., in 2000 and

Emsley et al., in 2007 showed the major results were drastically positive correlations of prolonged DUP with a slower reduction of psychotic episodes and intensity of positive and negative symptoms and partly also with quality of life, numbers of readmissions and global functioning. This suggests that a late treatment of the first psychotic episode prolongs the remission of the episode. Nevertheless, it should be remembered that a prolonged prodromal stage is associated with a prolonged duration of the first episode compared with acute psychotic episodes not preceded by a prodrome.

Addington et al., in 2004 Loffler & Hafner, in 1999 have confirmed the results from short-term follow-up studies that a positive association between DUP and increased positive symptoms. But Haan et al. in 2003 found a considerable correlation only with negative symptoms over six years. Bottlender et al. in 2003 found a significant correlation with both positive and negative symptoms over a period of 15 years. Harris et al. in 2005 by a naturalistic study with 318 first-episode patients followed up for 8 years after initial treatment, found a reasonable positive correlation between DUP and severity of positive symptoms and reduced social and occupational functioning, but no association between negative symptoms and DUP.

In 2005, Emsley et al., found no association between DUP and neurological irregularities as measured by the Neurological Evaluation Scale (NES) in 66 medication-naïve patients from an early-psychosis unit. Available studies of patients treated with neuroleptic medications or without treatment information are not informative.

The relationship between neuropsychological test and DUP outcomes are negative according to most of the studies because of the cognitive impairment runs a constant course more or less autonomous of the symptoms dimensions and in addition they are not clear constantly across the studies. In 2007 Lappin et al., found a positive association between DUP and decreased verbal IQ, verbal working memory, and verbal learning, but information on management was not given. Robinson et al., in 1999 found no relationship between neuropsychological test and DUP.

Study reviews and meta-analysis related to the outcome parameters purely indicating a tendency of consistency than simple studies. In 2005, Perkins et al., by meta-analysis, based on their 43 publications, they concluded that a short DUP is disapprovingly related with global psychopathology, functional outcome and positive and negative symptoms, that this relationship seems to be independent of the effects of other factors, and that DUP does not seem to be related with symptom

dimension of neuro-cognitive functions. He also stated that there is no relationship with abnormities of brain morphology, even though there is little evidence for this conclusion.

In 2005, Marshall et al., carefully reviewed 26 studies published up to 2004 and found no association between DUP and first clinical valuation of psychopathology and social performance. The significance of correlation is increased with a lengthening follow- up period from 6 months to 12 or 24 months in almost all studies. The effect of DUP appeared strong even after calculating for premorbid adjustment in 12 studies and this was affirmed by Sing in 2007. From 10 Studies published between 1992 and 2000, it is stated that although there shows some evidence for an association between DUP and first effect to antipsychotic treatment, the strength of these findings and their independence form confounding variables are hitherto to be established, Norman and Malla (2001).

Whether reducing DUP by timely treatment is able of warding off adverse consequences of the disorder is clinically a crucial question. Controlled intervention studies in beginning of illness and with adequately long follow-up periods are essential to ascertain whether it is the period of the dynamic disease process prior to the starting of an

efficient treatment or an adverse type of the disorder, pointed out by an insidious onset which actually predicts a poor outcome.

Few studies of controlled trials, low-dose neuroleptic medication and/or cognitive-behavioral therapy of early positive symptoms with prodromal stage patients and at augmented or ultra-high psychosis risk of diverse definitions have constantly stated weak, but appreciably encouraging, treatment effects on symptoms and a decline in transitions to schizophrenia (French et al., in 2007; Lewis et al., in 2002; McGorry et al., in 2002). The long-term illness course effects are not yet recognized. In summing up, at this period of time these studies can be seen as simply signifying that early interference administered in the first episode can have benign effects.

As observed by Marshall et al, The reason for this timely treatment is not just caring (to reduce the period of untreated distress) but a rising detection that the duration of untreated psychosis will have a major force both on direct progress rates and on long-standing outcomes and disability.

Larsen *et al* and Birchwood et al noted that an independent effect of the DUP on outcome was attributed to a direct `neurotoxic' effect and to a `critical period' in personal development when people may miss out on vital social development and may obtain disabilities and patterns of

behavior with long-term cost. The relationship between the DUP and outcome give some support for its use as a service-level prognostic measure in new onset schizophrenia.

In 2006, Mcglashan observed that DUP is an appropriate measure only of the early recognition and function of early intervention services. The most important factor of relapse is the period of illness earlier to initiating antipsychotic medications as observed by the Northwick Park trial of First episode schizophrenia patients.

It was Wyatt's decisive analysis (1991) of antipsychotics and the natural course of the schizophrenia that definitely established the significance of the extent of untreated psychosis as a predictive marker.

Short DUP was not only related with better 'treatment receptiveness' but also with better decline in negative symptoms, an appealing decision given that negative symptoms are decided less responsive to antipsychotics than positive symptoms.

Clarke et al in 2006 a new study has even attempted to demonstrate the consequence of DUP on outcome, reporting that each component raise in DUP is associated with a 7.8 point augment in global functioning scores and a 1.9-point add to in positive symptom scores which assess illness course without calculating treatment. Acute treatment studies of

the first episode of psychosis, mainly patients diagnosed with schizophrenia (May et al) shown parallel results.

Craig TJ et al (2000) study of duration of untreated psychosis and 24-month clinical outcome in a first admission patient series do not hold up the proposal of a psycho-toxic effect of extended exposure to untreated psychotic illness.

WHO multi-national studies:

IPSS1968-International Pilot Study of Schizophrenia: This found that higher proportion of patients in India, Colombia and Nigeria had better outcome on most dimensions than patients in developed countries at 2 and 5 years follow up assessment.

WHO 10 countries study, in which epidemiological cohorts of first episode cases were uniformly assessed upon their first contact with community or hospital services, the better course and outcome in developing country areas could not be attributed to any particular clinical subtype of the disorder.

The main outcome difference across the study areas was in the average length of symptom free remissions. Analysis of the data revealed that the better overall pattern of course and the less disabling outcome in the study areas in developing countries were mainly attributable to a significantly greater percentage of patients remaining in remission of

symptoms over long periods after an acute psychotic episode rather than to milder or shorter psychotic episodes.

DOSMED-study of Determinants of Outcome of Severe Mental Disorder, and ISOS-International Study of Schizophrenia (ISOS) were showed better outcome when the DUP is shorter in developed countries.

Indian studies on duration of untreated psychosis and outcome:

In 1981, multi centered trial conducted in India by ICMR (Indian council of medical research), SOFACAS -Study of Factors Associated with Course And outcome in Schizophrenia, in lucknow, Vellore, and madras at the end of 2 and 5 years of follow-up. Outcome assessment was done which showed factors significantly associated with good overall outcome are;

1. Short duration of illness
2. Regular treatment compliance
3. Patient not perceived unsafe by others
4. Not avoiding patients by others
5. Absence of financial difficulties
6. Higher socioeconomic state
7. Lack of hazardous behavior
8. Rural setup and Higher religious activities
9. Absence of schizoid traits.

Kulhara et al., 2000, stated that schematic psycho-educational services were associated with improved outcomes than routine out patient treatments.

Study by N. Srinivasan tripathi et al., in 2004, 75 patients with schizophrenia (never- treated) found in a community survey in Chennai, 49 managed with antipsychotics were followed up continuously for one year period and found that a good clinical, social and global outcome in about one third of patients ,and occupational outcome in half of the patients was observed. Patients with poor global outcome were not different from those with good outcome on demographic and clinical factors but for the presence of formal thought and delusional disorder. The fraction with good outcome in clinical, work and global measures decreases constantly with increasing DUP. This divergence was important for clinical and global outcomes after a DUP of 5 years.

In 2006 Rathi Mahendran et al., found that Psychiatric co-morbidity in first occurrence schizophrenia is correlated with worse prognosis in hospitalized patients of first occurrence schizophrenia by a longitudinal two year follow-up study. This emphasis that the need for early finding and treatment of these comorbid conditions.

Another Indian and Canadian study during 2010 by Srividya N. Iyer et al compared the various outcomes of first episode psychosis in

India with Canada. The results showed a major improvement over time in patients in India, than their counterparts in Canada for negative symptoms and functioning when age and marital status are held constant. But the positive symptoms and psychopathology in general did not show this time-by-place interaction. From this study we can come to a conclusion that the outcome initially in the course of schizophrenia can be influenced by socio-cultural context of the treatment.

Chatterjee et al., 2010 observed that treatment in the initial part of schizophrenia predicted an improved outcome through higher literacy rate, minimal initial symptoms, family involvement, medication compliance and community involvement (Self Help Groups) by their study involving 256 patients followed up for 4 years in rural part of Goa.

A prospective trial of DUP and outcome of patients never- treated was done by Jagadish Thirthalli et al in 2011. They found that in India the delay in getting treatment among psychotic patients is extensive. Longer DUP is related to poorer outcome in psychopathological and functional components.

Isaac and Padmavathi et al., in 2007 studied the factors causing good prognosis of schizophrenia in low- and middle-income countries (LAMI). They observed a negative correlation between DUP and income in LAMI countries. The treatment cost is a barrier to care and financial

support for antipsychotic medications would augment the contact to treatment and outcome of psychotic disorder in LAMI countries.

Factors shown to be associated with better prediction of psychosis in low- and middle-income countries:

Well-known factors:

- a reduced amount of emotion expressed
- superior social support
- Tolerating strange behavior by the family and society
- Marital status

Factors those are uncertain:

- Low level of urbanization and industrialization
- Early demise of those with worst outcome
- Higher prevalence of acute schizophrenia

Family studies:

Family studies clearly demonstrate that the risk of developing schizophrenia is increased in the relatives of patients. It is higher in siblings and even higher in children of probands, reaching a life time risk 10% or more. This equates about the same morbidity risk, when a

population prevalence of the disorder of 1 % is assumed. The lower risk among parents can be explained by the reduced reproductive fitness associated with schizophrenia. Illness among parents is found mainly in those who become ill after having children and those who have a milder version of the illness, which might not satisfy the diagnostic criteria for disorder. In addition it is possible that the de novo mutation events might contribute to this anomaly. Among many studies, 2 studies showing significantly higher morbidity risk in relatives of patients compared with relatives of controls. The morbidity risk in first degree relatives of schizophrenia varied widely from 1.4 to 6.5%, and in controls from 0 to 1%.

Factors those need further studies:

- Co morbid use of substance
- Duration of untreated psychosis (DUP)
- Interventions by medications

Possibility of measuring DUP:

Clinically it is hard to identify this time when a particular symptom or behavior makes the person form a non-psychosis to a psychosis domain as suggested by Moller in 2001.

The time between the first sign of psychotic illness and emergence of elaborate psychotic symptoms to duration between emergence of symptoms of psychosis to starting of treatment is different (Day et al, 1987).

Few methodological and conceptual problems hamper the measuring of DUP retrospectively. So the measurement of DUP is frequently methodologically challenging one. DUP is often retrospectively defined, and the recall bias can be reduced by many sources such as medical records and detailed interviews with relatives.

Determinants of DUP for an individual:

When assessing the possibilities of shortening DUP and what the effects could be of this possible change in the length of DUP, it is critical to know what factors predict and relate to either short or long DUP.

Previous studies have shown that subjects who are living alone or homeless and unemployed have longer DUP (Barnes *et al.* 2000, Chen *et al.* 2005, Oliveira *et al.* 2010), whereas the effects of acute onset and history of psychosis in the family seem to shorten DUP (Chen *et al. in* 2005, Compton *et al. in* 2008). The effect of living with family and the involvement of family in help-seeking on the length of DUP are unclear (Morgan *et al.* 2006 and Compton *et al* 2008). Compton et al., 2011 in

their study observed that living with family members and poverty was linked with longer DUP.

Chong *et al.* (2005) evaluated the reasons for not seeking a psychiatrist and observed that besides the unknown reasons, there were two important reasons:

1. Not recognizing the presence of problem, and
2. The idea of problems attributed to supernatural or mystical reasons.

The lack of knowing or finding other explanations for odd symptoms may not be that uncommon in Western societies either, although the finding was from an Eastern population. Studies by Burns, 2012 and Cascio et al., 2012 found either gender or cannabis use is not related to the prolongation of DUP.

Determinants of DUP regarding the health-care system

Determinants of DUP may be divided into two different types. One type of cause for delay in initiation of treatment is due to avoiding of treatment initiation as long as possible. Another possible cause is defect in health care system that made the delay in initiation of treatment. In most developed countries, psychosis is treated quickly and efficiently. Though, for a variety of reasons such as economic limitations, in developed countries not all requirements for treatment of psychotic

people may be met either and this is even worse in developing countries (Chiliza *et al., in* 2012).

When does DUP end?:

The end of the DUP is theoretically easy to date, but `the commencement of treatment' is in realism an equally compound construct. Does `untreated psychosis' stop when any form of treatment begins, when treatments with antipsychotic medications are started, when treatment at an optimal dose has been stick to for a sufficient duration, or when the disease itself abates? Many trials do not formulate these differences understandable in their measure of DUP and treatment adequacy is not clearly defined in the scales used for those studies. In 2005, Singh et al., observed that in clinical practice, some clinicians start antipsychotic treatment in the prodromal stages of the illness. How can DUP be measured in that type of cases? When starting the treatment, at the onset of psychosis with prominent mood symptoms should treatment with mood stabilizers or antidepressants without antipsychotics be considered for treatment and therefore the end of the DUP?

Rating scales of DUP:

Some rating scales were developed to record the commencement of psychosis retrospectively. In 1993, Beiser *et al*., developed a checklist of behaviours outlining the evolution of initial appreciable symptoms,

appearance of psychosis and beginning of treatment-seeking. In 1992, Hafner et al., developed IRAOS-Interview for the Retrospective Assessment of the Onset of Schizophrenia. IRAOS is a form of interview to evaluate symptoms, socio-demographic distinctiveness and psychological impairment in the time course of emerging psychosis.

The Nottingham Onset Schedule (NOS) developed by Singh et al in 2005 is short form of interview with leading questions. It is a rating scale to calculate the commencement in psychosis. According to this scale the onset of psychosis is comprising of (1) a prodromal period of two parts, one is a period of `discomfort' and another following period by `non-specific' symptoms; (2) emergence of psychotic symptoms; and (3) a upsurge of specific symptoms directing to a precise diagnosis.

The NOS gives a normalized and consistent ways of recording of initial changes in schizophrenia and finding fairly accurate time points for calculating several durations in budding psychosis.

This scale permits for many ways of to measure and to define delay in treatment by changing the beginning point of onset, including period of untreated illness (the time period between prodromal symptoms to treatment), period of untreated emergent psychosis (the time between first symptom of psychosis to treatment) and duration of untreated established

psychosis (the time between manifestation of fully fledged syndrome of psychosis to treatment).

To assess the result of early treatment services is DUP a suitable marker?

Craig et al, 2004 and Petersen et al, 2005 demonstrated in their trails that specialised early treatment services are more successful than routine care in promoting clinical outcomes and adherence of treatment.

In 2002, McGorry et al, concluded that combined therapy of risperidone with psychotherapy decreased the risk of developing full-fledged psychosis from their randomised controlled study in a high-risk prodromal population.

A study project conducted by Melle et al., in 2004 and Friis and Johannessen et al., in 2005 in Denmark and Norway, compared outcomes in patients with first onset psychosis diagnosed by an early intervention team, with those seeking treatment in another area without early intervention facilities but with same healthcare services. Finally they found that patients entering the early treatment had decreased DUP of five weeks and better prognosis at three months.

However a study conducted in London by Malla et al., in 2005 compared previous to and subsequent to the implement of an early intervention programme in treating patients with schizophrenia but they

did not detect any fall in DUP following this initiative program. But they argued that improving general practitioner skill in detecting and treating psychosis with novel antipsychotics results in milder illness. Therefore, the support for the usefulness of early case finding services in shortening DUP seems to be limited.

DUP and recovery:

The DUP estimate low recovery even after treatment for three months after confounding other markers of DUP and the severity of the disease at baseline.

Recovery effect results from early case finding and early treatment which reduce DUP from six months to one month and outcome from 6 years to one year.

Thara et al., SCARF-Schizophrenia Research Foundation, Chennai based had conducted a study to know the impact of early intervention service within 6 months of emergence of psychosis to the outcome in 2003. At the end of one year 80% of patients obtained full recovery and showed very few cognitive defects.

These highlight the significance of implementing a well-organized community recognition and referral system, with timely delivery of efficient treatments, particularly for patients with first onset schizophrenia.

Confounding variables associated with DUP:

After correcting the effects of other factors DUP remained an important indicator of outcome. Functional outcome seemed to decrease considerably even with short treatment delays of more than a week, with more progressive worsening in functioning after very long DUP of more than a year. This outcome was related variably with pre-morbid modification of factors like female gender, presence of affective disorder, period of prodromal stage, and treatment with Early Psychosis Prevention and Intervention methods.

Barnes et al., 2000 and Verdoux et al., 2001 in their studies confounding factors like age at onset, sex, premorbid condition, mode of onset and socio economic status are used to assess the Long DUP was associated with delayed treatment. Premorbid condition and mode of onset therefore denote built-in mechanism of psychotic illnesses interrelated to a shortened DUP, whatever the early intervention efforts. Singh et al., 2004 stated that even though acute onset is related with a short period of first episode, is not an independent indicator of outcome in psychosis when sex and premorbid functioning are confounded. To summarize, DUP is an important indicator of outcome even after correcting the impact of these confounding factors.

Gender:

Lobel et al 1992 and Larsen et al 1996 reported that males have a long duration of untreated psychosis than females but five other studies do not find any gender difference to be associated with outcome.

Age at onset:

Ho et al., (2000) in their follow up studies observed that longer DUP was appreciably associated to onset at younger age while many other studies failed to show any such difference.(Hans et al, Lobel et al, Larsen et al, Blake et al.)

Symptoms at base line:

Higher level of symptoms at presentation of illness like negative and positive symptoms have associated with prolonged duration lf DUP in many studies (Larsen et al, Browne et al, Malla et al, Blake et al). Some studies showed the prolongation of DUP was associated only with the severity of negative symptoms but not with that of positive symptoms or general psychopathology severity. Drake et al notified a relationship between prolonged DUP and higher positive but not negative symptoms at presentation, but others have found no relation to initial positive symptoms (Larsen et al, Malla et al).

Premorbid adjustment:

In 1896, Kraepelin stated that a substandard psychosocial activity is a risk factor for developing schizophrenia. This is also supported by Gittelman and Klein in 1969, that is low intellectual and psychosocial performance before the onset of psychosis is associated with poorer short and long term outcome.

Poor premorbid functioning is related to higher severityof overall symtomatology, social execution , negative symptom domain and early onset of schizhphrenia in 1998 by Malmberg. A.

Poor premorbid adjustment is autonomously related with both DUP and worst outcome. Poor adjustment delays access to health care, and consequently aggravating the risk of developing with a non-remitting course of psychosis. In 2008, P. Jeppesen et al, in their studies showed that poor pre-morbid adjustment is correlated autonomously with more negative symptoms and adverse social outcome.

Response to treatment:

Shorter DUP was linked with a superior response to anti psychotic medications as calculated by improvement in severity of symptoms, studied by Ucok.A and Polat A, in 2004.

Outcome in schizophrenia in fraction:

Approximate guide to course and prognosis at 13 years follow up.

1. 15 to 20 % first episode will not recur
2. Few people will remain in an employment,
3. 52 % are without psychotic symptoms in the last 2 years
4. 52 % are without negative symptoms
5. 55 % show good/fair social functioning

Poor Prognostic factors:

Poor premorbid adjustment

Insidious onset

Onset in childhood or adolescent

Cognitive impairment

Enlarged ventricles

Hebephrenic schizophrenia

Family history of schizophrenia

Male sex

Good prognostic factors:

Female sex

Acute onset

Married persons

Marked mood disturbances, especially elation during initial presentation

Family history of affective disorder

Catatonic schizophrenia

Presence of precipitating stressors

Living in developing countries.

AIMS AND OBJECTIVES

1. To evaluate the influence of duration of untreated psychosis (DUP) on the short term outcome

2. To evaluate the influence of DUP with severity of the symptoms at beginning of the first treatment.

3. To assess the association of premorbid social adjustment on DUP.

NULL HYPOTHESIS

1. No association between improved and unimproved groups in terms of DUP.

2. No association between severity of symptoms at baseline and duration of untreated psychosis.

3. No association between modes of onset, socio demographic factors with DUP

4. No association between premorbid social adjustment and DUP

MATERIALS AND METHODS

This study was done at the Institute of Mental Health, Chennai.

SAMPLE:

60 consecutive patients who were all admitted as in-patient in the institute of mental health, fulfilling the ICD 10 criteria for schizophrenia those were all diagnosed to have first episode and drug-naïve patients.

INCLUSION CRITERIA:

1. Age 18 - 45 years.
2. Patients with schizophrenia fulfilling ICD-10 criteria for diagnosis.
3. Drug naïve patients.
4. First episode.

EXCLUSION CRITERIA:

1. Psychiatric disorders due to general medical condition
2. Other primary psychiatric disorders
3. Substance induced psychotic disorder
4. Comorbid substance use
5. History of head injury.
6. Mental retardation and Epilepsy.

MATERIALS USED

1. Semi structured proforma.
2. Detailed Clinical interview.
3. PANSS-Positive And Negative Syndrome Scale.
4. Clinical Global Impression Scale (CGI-Severity, CGI-Improvement).
5. Premorbid Social Adjustment Scale (PSA Scale)

Semi-structured Proforma:

This was developed by including the socio demographic and clinical data, family history, subtypes of schizophrenia, DUP, mode of treatment, and duration of hospitalization. (Appendix I)

Clinical interview

Detailed clinical interview was done to diagnosis schizophrenia which fulfills ICD-10 criteria.

Patients and their care givers were interviewed in detail about the history of onset of illness, initial behavioral changes, any type of initial treatment and prodromal symptoms by providing privacy to the patients.

Determination of Duration of untreated psychosis:

The determination of duration of untreated psychosis was done clinically by a detailed interview with the patient and their care givers. Prodromal symptoms were cautiously elicited and the beginning of

symptom of first-discomfort or change in behavior was obtained, it may be positive or negative symptom which decided the onset of psychosis.

The evaluation of DUP incorporated the following,

1. Positive symptoms like hallucinations, thought disorder, odd beliefs, and delusional disorder.
2. Negative symptoms like depression, lack of interest and motivation, loss of energy and loss of interest.
3. Social decline like social withdrawal, poor interpersonal relationship, social evasion, and anhedonia.

Outcome measured from clinical improvement after 12weeks of followup.

Positive And Negative Syndrome Scale :

It is a drug-sensitive tool which gives balanced illustration of Positive and Negative symptoms and measures their association to each other and to global psychopathology. This scale comprises of following subtype namely.

1. Positive scale (seven items),
2. Negative scale (seven items),
3. General psychopathology scale (16 items) and
4. Profile summary. This includes

a) positive syndrome: sum of P1 to P7,

b) negative syndrome: sum of N1 to N7,

c) composite index: Positive minus negative,

d) general psychopathology: sum of G1 to G16, and

e) cluster scores of

Anergia: a sum of N1, N2, G7, G10,

Thought disturbances: a sum of P2, P3, P5, G9,

Activation: a sum of P4, G4, G5,

Paranoid: a sum of P6, P7, G8, and

Depression: a sum of G1, G2, G3, G6.

In addition to interpretation of scale scores, percentile is also assessed by dividing raw score with total score.

Interpretation of the percentile score:

Above 95	-	Symptom severity is Very high
75 to 94	-	High
26 to 74	-	Average
6 to 25	-	Low
5 and below	-	Very low

At the time admission PANSS scale assessed and the severity of the symptoms measured. Follow up assessment done at 12 weeks.

Clinical global impression scale:

The CGI-S (Severity) is adapted from the CGI scale developed by Guy.W in 1976. The severity of the symptoms assessed with this scale at the time of admission. This is observer- rated clinical experience scale which measures the severity of the illness by 7 point items. CGI-S severity of illness score corresponds to PANSS score by the following points.

CGI-S scale		PANSS score
Mildly ill	-	58
Moderately ill	-	75
Markedly ill	-	95
Severely ill	-	116

CGI – Improvement scale (CGI-I) is also a 7 point item scale. This is used to assess the treatment response of symptoms presented at the baseline of illness. This rates from 1 (very much improved) to 7 (very much worse).

The Premorbid Social Adjustment Scale:

Premorbid period is assessed one year before the onset of the illness by interviewing the care-giver. This scale is a 7 point-item scale modified from Cannon-Spoor scale (1992).

Range from 0-good adjustment to 6-poor adjustment. It is used to evaluate the premorbid functioning in four stages of life from early

childhood (0-11yrs), early adolescent (12-15 yrs), Late adolescent (16-18 yrs) to adulthood (19 and above) with assessing in the five areas of

1. Sociability and withdrawal,
2. peer relationship,
3. adaptation and interest in school,
4. scholastic performance,
5. social and sexual aspects (from Early adolescent to adulthood).

Each item is separately scored for four stages from 0-6 and total score in calculated by summing up the scores obtained. The possible score is the highest score derived by summing up the maximum score for all items.

The subscale score is calculated by dividing the total score by the possible score. The Overall score ranges from 0 – 1 which is finally derived by averaging all the subscale scores. High overall score indicates poor premorbid functioning.

METHODS

Patients fulfilling the ICD-10 criteria for schizophrenia, admitted as in-patients in the Institute of Mental Health were evaluated. Those satisfying the inclusion and exclusion were taken in to the study. The diagnosis was obtained from case records and confirmed by 2 psychiatrists; one of them is senior consultant.

Informed consent in the written form was obtained for participation in the study from patients as well as their care-givers.

The patients were given the semi-structured proforma, PANSS-Positive and Negative Syndrome scale, CGI-S: Clinical Global Impression Severity scale and Premorbid Social Adjustment Scale –PSA at the time of admission.

Treatment in the ward was given by the psychiatrist in-charge of the ward depending upon the patient's symptoms severity. Treating psychiatrist was completely blind to the study sample.

Follow-up assessment was done after a period of 12 weeks by administering PANSS and CGI-S. All those who completed 12 weeks of follow-up were enquired from their care givers about compliance to medication.

The outcome was assessed using CGI-I (Improvement). The outcome variable was converted into dichotomous, unimproved

(4 or more than 4 which includes no change, minimally worse, much worse, and very much worse) and improved (less than 3 on CGI-I which includes minimally improved, much improved, very much improved).

The data collected thus were tabulated and discussed with reference to aims and objectives of the study. Statistical analysis was done using chi-square test, t-test, and correlation methods. In measuring DUP more chance of right skew, hence after initial data analysis DUP was normalized by taking the log to base 10 to allow the use of parametric statistics (Pearson's r, t tests) and these results were presented. Data was analyzed using SPSS 22.0. $p<0.05$ is considered as a statistically significant value.

Approval was obtained from the ethics committee, Madras Medical College, Chennai.

RESULTS

60 consecutive patients were screened, evaluated and entered in to the study.

At the end of 12 weeks follow up assessment was done. 58 patients reported along with their caregivers for follow-up assessment. Remaining 3 patients were excluded, one patient was found to be HIV positive and 2 patients were found missing from the ward. .At the end of 12 weeks follow-up assessment was done for all 57 patients reported along with their caregivers.

Sample characteristics at admission (n=57)

Baseline sample included 57 patients among which 75.8% were men and 24.2% were women. More than 90% of the patients were in low and middle socioeconomic status.

7% were uneducated, 15.8% up to primary school, 42.1% up to middle school, 21.1% up to secondary school, 8.8% were diploma, and 5.3% were graduate. 31 (54.4%) were unmarried, 24 (42.1%) were married, 2 (3.5%) married and separated. 46 (80.7%) were in a joint family system, 11 (19.3%) in a nuclear family system. 29 (50.9%) were unemployed and 28 (49.1%) were employed among the sample.

TABLE 1

MEAN OF THE WHOLE SAMPLE (N=57)

Variables	N	Mean	Std. Dev	Min	Max
Age	57	31.82	6	19	42
Duration of untreated psychosis	57	3.02	3	.25	10.00
Age of onset of Illness	57	28.46	6	17	38
Duration of hospitalization (days)	57	31.30	23	10	90
Panss positive syndrome	57	18.67	8	9	34
Negative syndrome.	57	19.74	8	7	39
General psychopathology	57	34.21	10	15	68
CGI-S Score	57	4.39	1	3	6
CGI-I Score	57	3.26	1	2	5
PMSA Score	57	.32	0	.0	.8

Age at onset of illness is 28.46 years; the mean duration of untreated psychosis was 3.02 years. 12 (21.1%) patient had a DUP between below one year, 18 (31.6%) patients had a DUP between 1 to 2 year, 27 (47.4%) patients had a DUP more than two years.

Family history Schizophrenia was present in 10 patients (26.3%). No family history of schizophrenia in 42 (73.7%).

In unimproved group at 12 weeks the DUP mean value is 1.65. In improved group at 12 weeks mean value is 4.92. The p value is less than 0.01 which is statistically significant.

Duration of hospitalization in improved group mean value is 24.70 days.In unimproved group mean value 28.9 both are statistically significant. (p=0.02)

TABLE NO 2

CORRELATION OF DURATION OF UNTREATED PSYCHOSIS WITH OTHER VARIABLES

		Duration of untreated psychosis
Age of onset of Illness	Pearson Correlation	-.072
	P-Value	.594
	N	57
Panss positive syndrome	Pearson Correlation	-.324
	P-Value	.014
	N	57
Negative syndrome.	Pearson Correlation	.177
	P-Value	.188
	N	57
General psychopathology	Pearson Correlation	-.037
	P-Value	.786
	N	57

There is positive correlation between PANSS positive symptoms and DUP ($p< 0.05$). There is no significant correlation between DUP and the age at onset of illness, negative syndrome, and general psychopathology.

TABLE NO 3

GENDER WISE COMPARISON BETWEEN

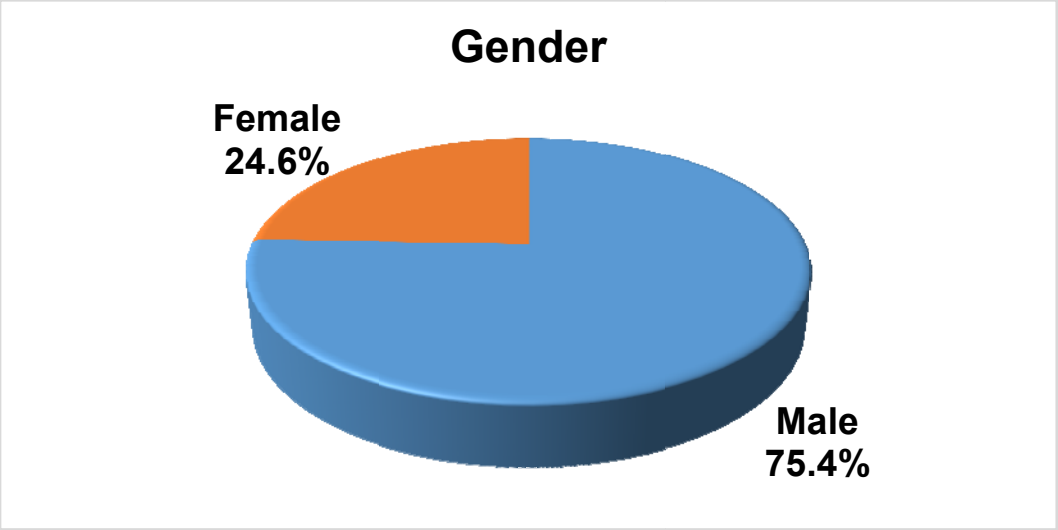
IMPROVED AND UNIMPROVED GROUPS

Gender	Outcome					
	Improved		Unimproved		Total	
	N	%	N	%	N	%
Male	25	75.8	18	75.0	43	75.4
Female	8	24.2	6	25.0	14	24.6
Total	33	100.0	24	100.0	57	100.0

Gender wise comparison between improved and unimproved groups

Among the improved group of patients 75.8% were males and 24.2%were females. In the unimproved group 75% were males, 25% were females. The difference was not statistically significant.

Chi-Square Test	Value	P-Value
Pearson Chi-Square	0.004	0.948


Gender
Female
24.6%
Male
75.4%

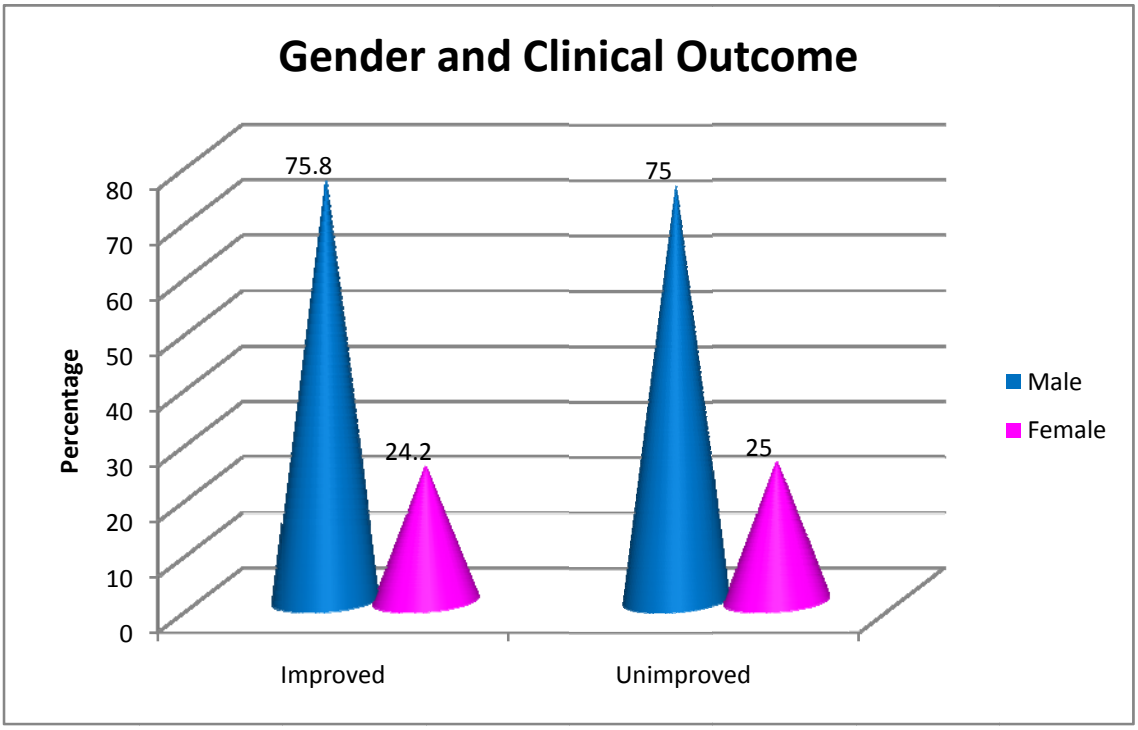

Gender and Clinical Outcome
Percentage
80
70
60
50
40
30
20
10
0
75.8
24.2
75
25
Improved
Unimproved
Male
Female

TABLE NO 4

COMPARISON OF GROUPS BY EDUCATION

Education	Outcome					
	Improved		Unimproved		Total	
	N	%	N	%	N	%
Uneducated	2	6.1	2	8.3	4	7.0
Primary	5	15.2	4	16.7	9	15.8
Middle	15	45.5	9	37.5	24	42.1
Secondary	7	21.2	5	20.8	12	21.1
Diploma	4	12.1	1	4.2	5	8.8
Degree	0	.0	3	12.5	3	5.3
Total	33	100.0	24	100.0	57	100.0

Comparison of groups by education

Chi-Square Test	Value	P-Value
Fisher's Exact Test	5.079	0.417

Among improved group, 6.1% were uneducated, 15.2% were educated up to primary level, 45.5% up to middle level, 21.2% up to secondary level, 12.1% diploma level.

In the unimproved group, 8.3% uneducated, 16.7% primary level, 37.5% middle school, 20.8% secondary level, diploma 4.2%, 12.5% degree level. The difference was not statistically significant.

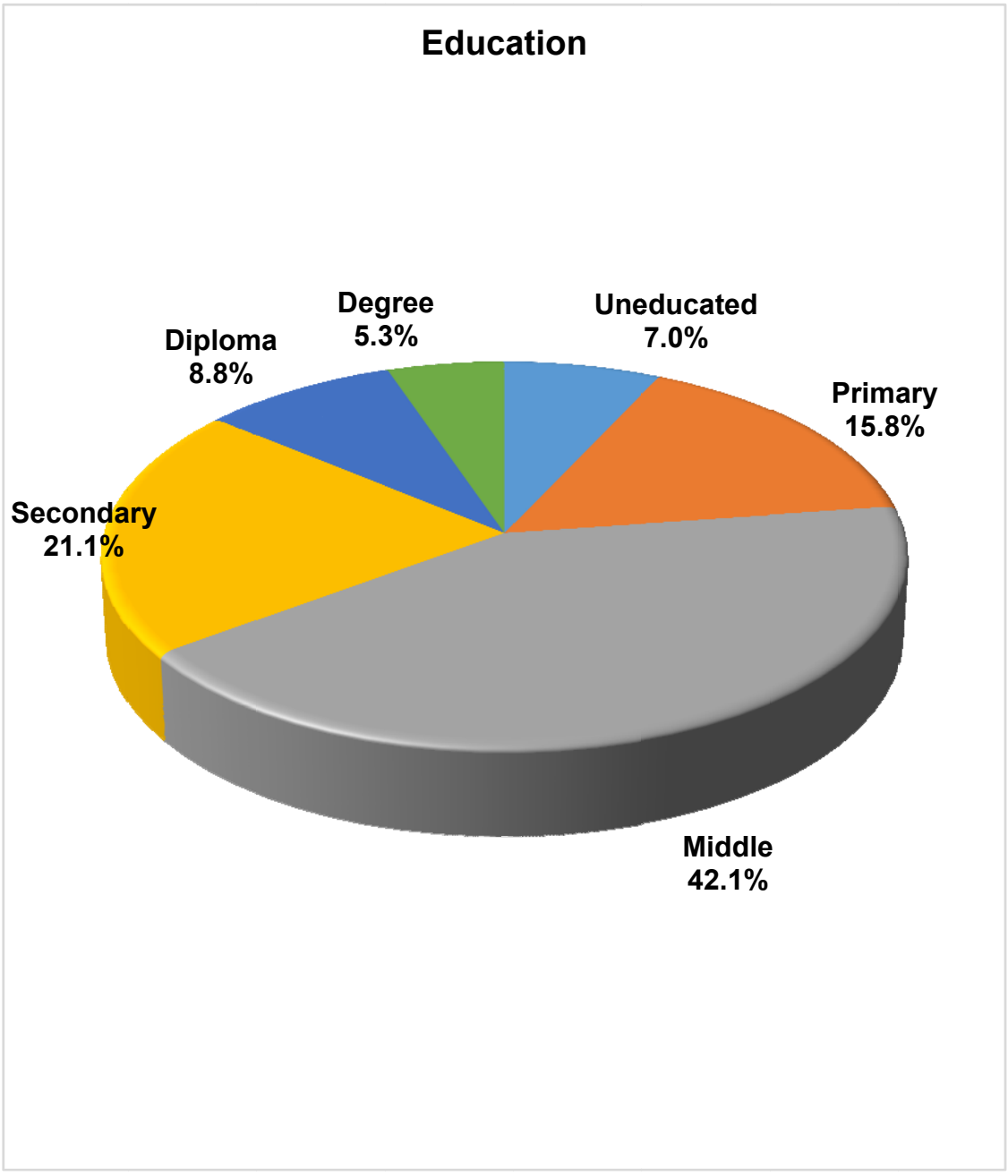

Education
Degree
5.3%
Uneducated
7.0%
Diploma
8.8%
Primary
15.8%
Secondary
21.1%
Middle
42.1%

TABLE NO 5

COMPARISON OF THE GROUPS BY EMPLOYMENT

Occupation	Outcome					
	Improved		Unimproved		Total	
	N	%	N	%	N	%
Unemployed	19	57.6	10	41.7	29	50.9
Employed	14	42.4	14	58.3	28	49.1
Total	33	100.0	24	100.0	57	100.0

Comparison of the groups by employment

Chi-Square Test	Value	P-Value
Pearson Chi-Square	1.407	0.236

In improved group, 42.4% were employed, and 57.6% were unemployed. In unimproved group 58.3% were employed, 41.7% were employed. This difference was not statistically significant.

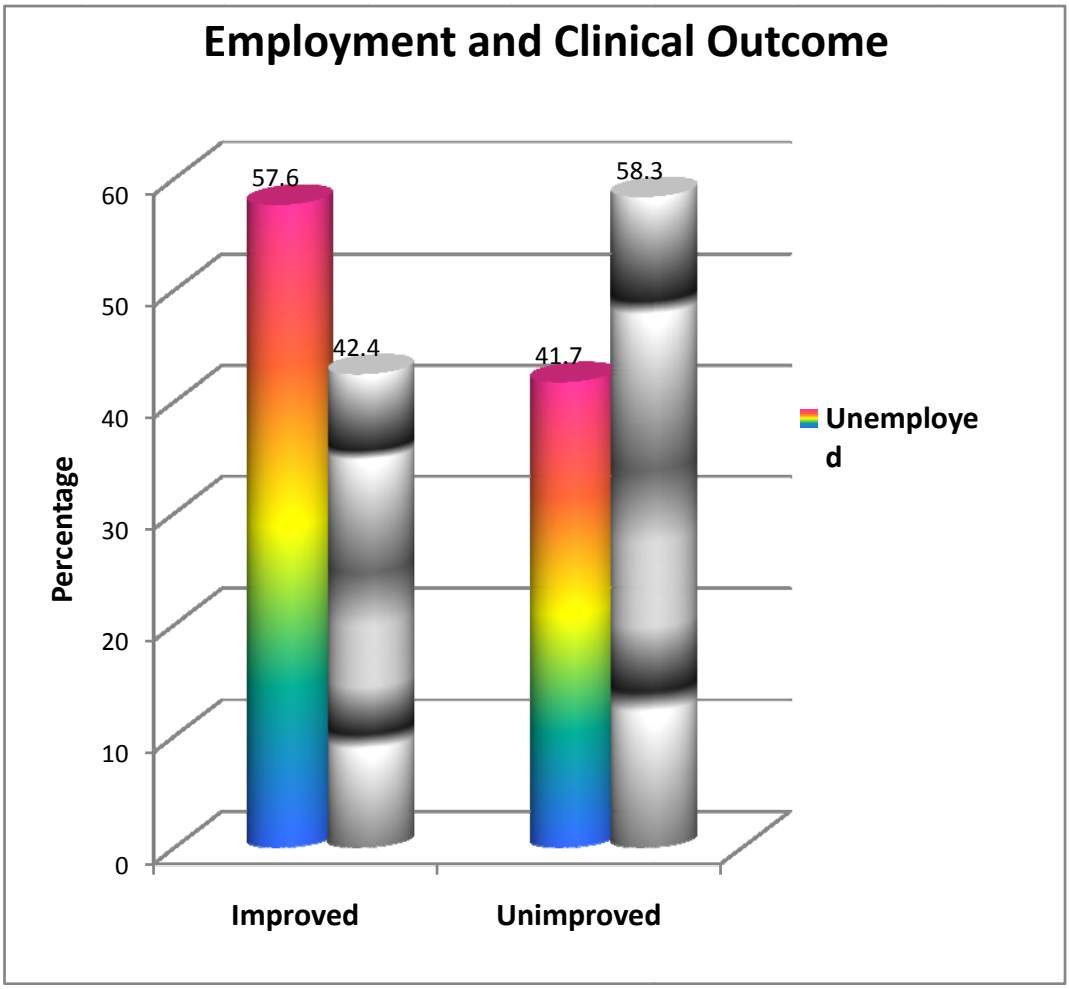

Employment and Clinical Outcome
Percentage
60
50
40
30
20
10
0
57.6
42.4
41.7
58.3
Improved
Unimproved
Unemployed

TABLE NO 6

COMPARISON OF THE GROUPS BY

SOCIOECONOMIC STATUS

Socio economic status	Outcome					
	Improved		Unimproved		Total	
	N	%	N	%	N	%
Low	26	78.8	20	83.3	46	80.7
Middle	6	18.2	4	16.7	10	17.5
High	1	3.0	0	.0	1	1.8
Total	33	100.0	24	100.0	57	100.0

Comparison of the groups by socioeconomic status

Chi-Square Test	Value	P-Value
Fisher's Exact Test	0.768	0.999

In the improved group 78.8% were from low socioeconomic status, 18.2% from middle socioeconomic status and 3% from high socioeconomic status.

In unimproved group 80.7% from low socioeconomic status, 17.5% from middle, and 1.8% from high socio economic status. The difference was not statistically significant due to this study done at Government institute, majority of patients are from the lower socioeconomic class.

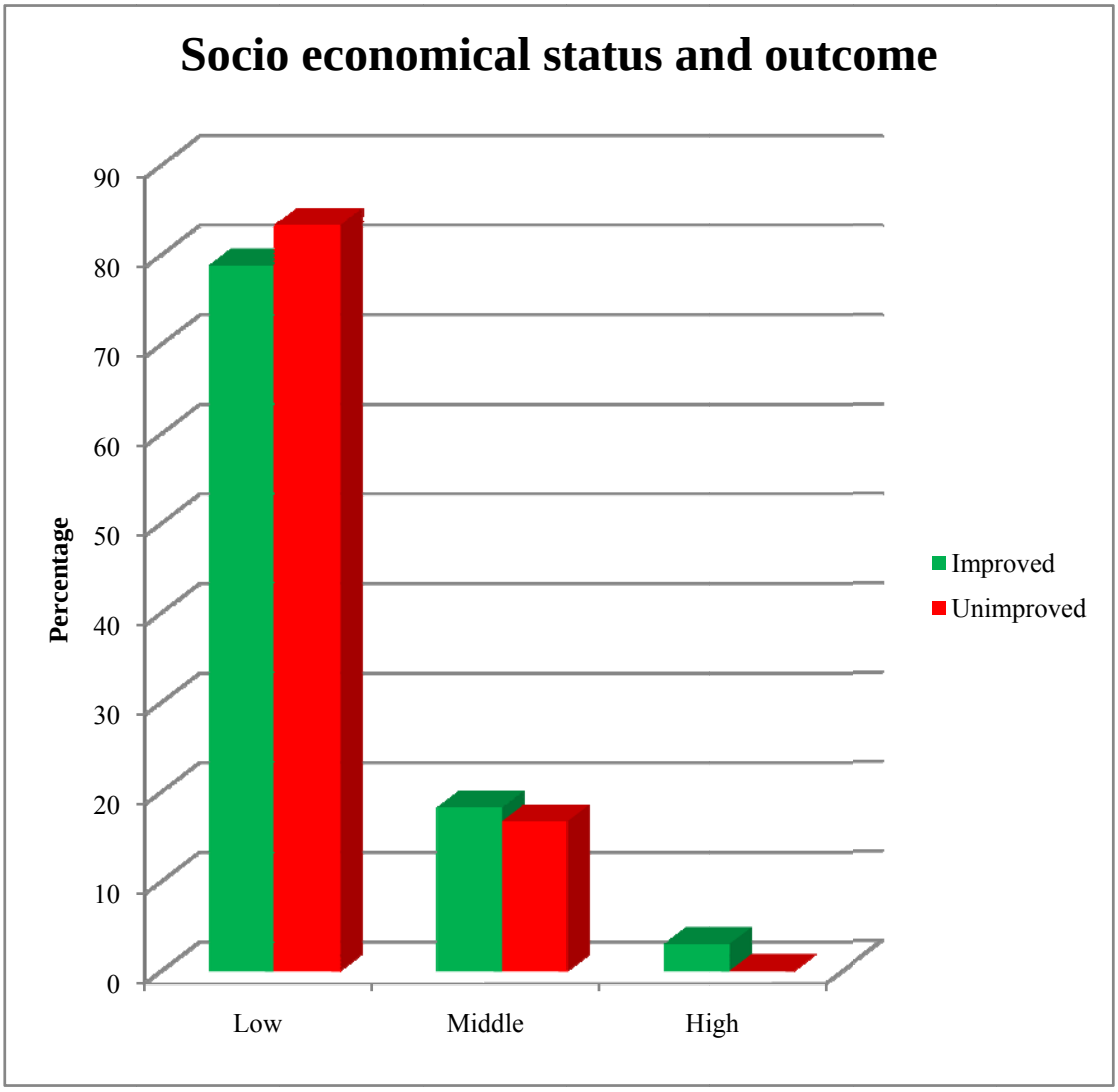

Socio economical status and outcome
Percentage
90
80
70
60
50
40
30
20
10
0
Low
Middle
High
Improved
Unimproved

TABLE NO 7

COMPARISON OF THE GROUPS –TYPE OF FAMILY

Type of family	Clinical Outcome					
	Improved		Unimproved		Total	
	N	%	N	%	N	%
Joint	27	81.8	19	79.2	46	80.7
Nuclear	6	18.2	5	20.8	11	19.3
Total	33	100.0	24	100.0	57	100.0

Comparison of the groups –type of family

Chi-Square Test	Value	P-Value
Pearson Chi-Square	0.063	0.802

In the improved group 81.8% belong to joint family, 8.2% belong to nuclear family. In the unimproved group79.2% belong to joint family, while 19.3% belong to nuclear family. The p value is 0.802 and the difference was not statistically significant.

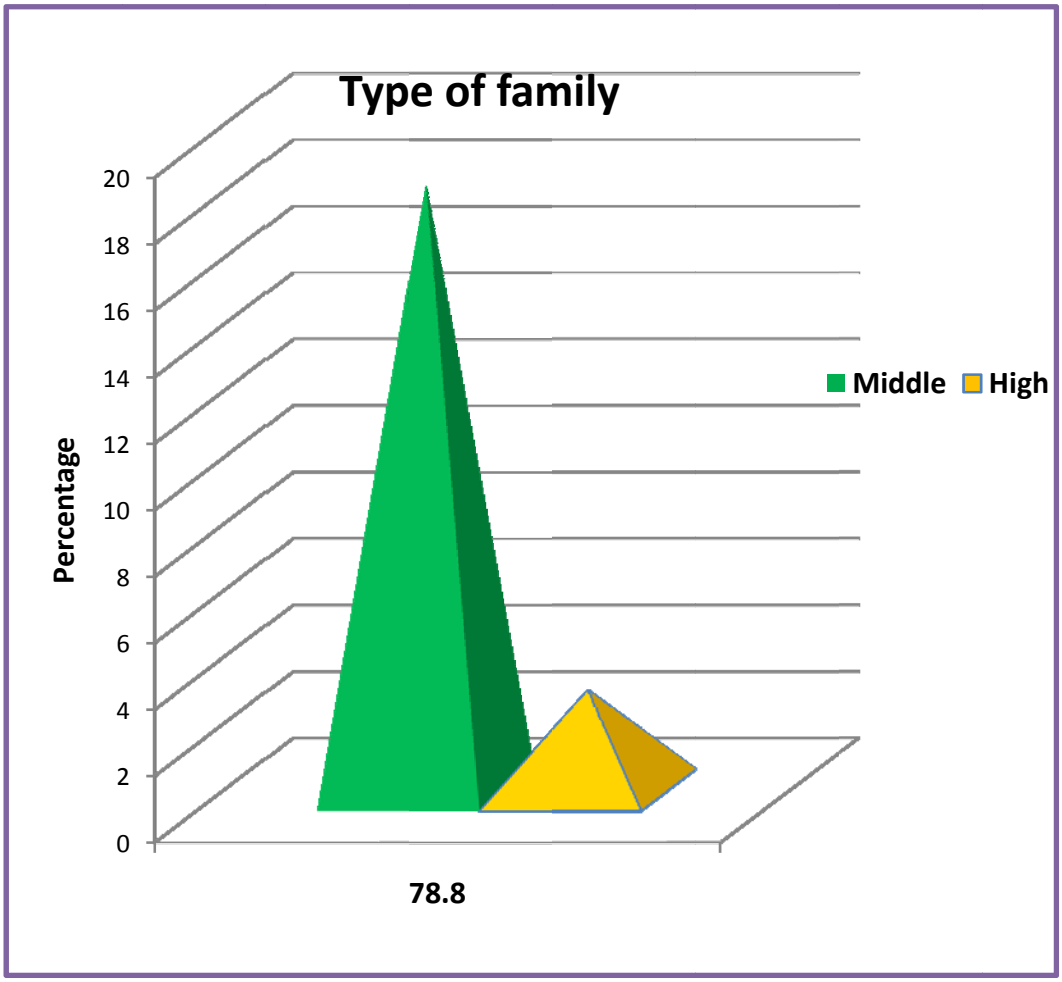

Type of family
20
18
16
14
12
10
8
6
4
2
0
Percentage
78.8
Middle
High

TABLE NO 8

COMPARISON OF THE GROUPS WITH

FAMILY HISTORY OF SCHIZOPHRENIA

Family history of schizophrenia	Improvement					
	Improved		Unimproved		Total	
	N	%	N	%	N	%
No	23	69.7	19	79.2	42	73.7
Yes	10	30.3	5	20.8	15	26.3
Total	33	100.0	24	100.0	57	100.0

Comparison of the groups with family history of schizophrenia

Chi-Square Test	Value	P-Value
Pearson Chi-Square	0.643	0.423

Family history suggestive of schizophrenic illness was present in 10 patients (30.3%) among improved group and in 5 patients (20.8%) in unimproved group. Since p value is 0.423, the correlation between the presence family history of psychosis and clinical outcome is statistically insignificant.

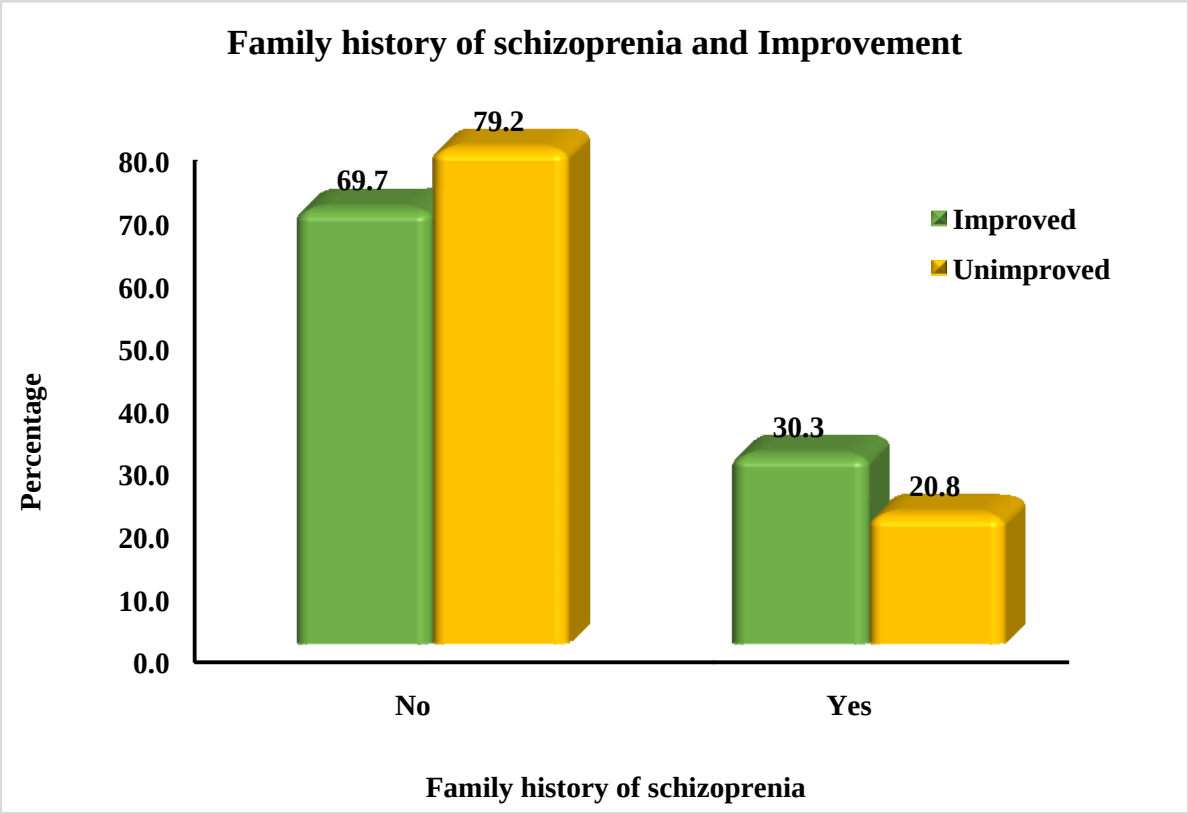

Family history of schizoprenia and Improvement
Percentage
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
69.7
79.2
30.3
20.8
Improved
Unimproved
No
Yes
Family history of schizoprenia

TABLE NO 9

COMPARISON OF GROUPS BY

SUBTYPES OF SCHIZOPHRENIA

Types of schizophrenia	Clinical Outcome					
	Improved		Unimproved		Total	
	N	%	N	%	N	%
Un differentiated	8	24.2	10	41.7	18	31.6
Paranoid	24	72.7	9	37.5	33	57.9
Hebephrenic	0	.0	2	8.3	2	3.5
Catatonic	1	3.0	3	12.5	4	7.0
Total	33	100.0	24	100.0	57	100.0

Comparison of groups by subtypes of schizophrenia

Chi-Square Test	Value	P-Value
Fisher's Exact Test	8.330	0.020

Among the improved group of patients, 24 patients (72.7%) were paranoid type. 8 patients (24.2%) were undifferentiated type, and one patient (3%) was catatonic type. In the unimproved group, 10 patients (41.7%) undifferentiated type, 9 patients (37.5%) paranoid type, 2 patients (8.3%) hebephrenic type, and 3 patients (12.5%) catatonic type. The p value is 0.02, the association is statistically significant.

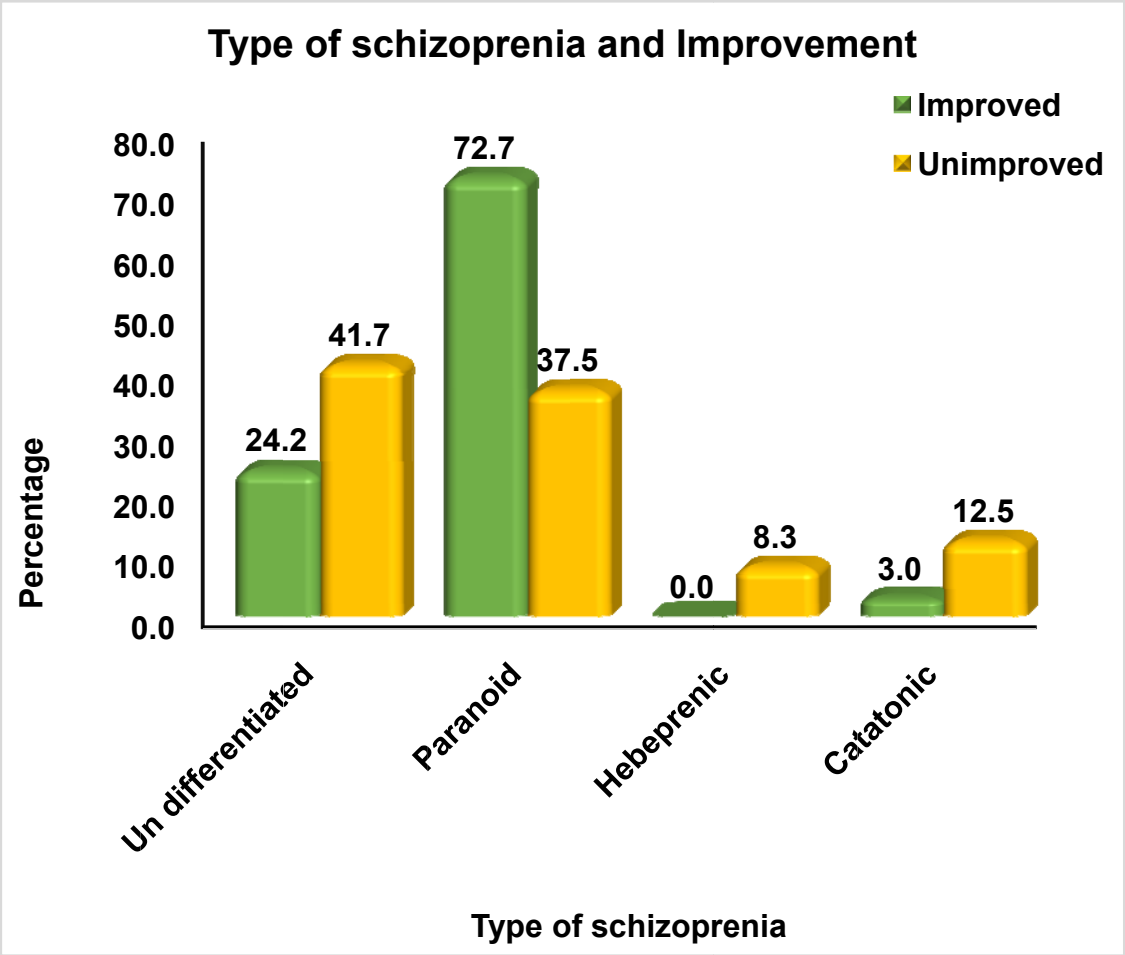

Type of schizoprenia and Improvement
Improved
Unimproved
Percentage
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
24.2
41.7
72.7
37.5
0.0
8.3
3.0
12.5
Un differentiated
Paranoid
Hebeprenic
Catatonic
Type of schizoprenia

TABLE NO 10

COMPARISON OF GROUPS BY HOSPITALIZATION

Duration of hospitalization (days)	Clinical Outcome					
	Improved		Unimproved		Total	
	N	%	N	%	N	%
≤ 15 days	14	42.4	5	20.8	19	33.3
16 - 30 days	15	45.5	11	45.8	26	45.6
> 30 days	4	12.1	8	33.3	12	21.1
Total	33	100.0	24	100.0	57	100.0

Comparison of groups by hospitalization

Chi-Square Test	Value	P-Value
Pearson Chi-Square	4.913	0.086

In the improved group, 14 patients (42.4%) were hospitalized for < 15 days, 15 patients (45.5%) were hospitalized for 16-30 days, and 4 patients (12.1%) for more than 30 days. In unimproved group 5 patients (20.8%) were hospitalized for <15 days, 11 patients (45.8%) were hospitalized for16-30 days and 8 patients (33.3%) were hospitalized for more than a month. Here, the p value is 0.086, thus showed no relation between these two groups in hospitalization for treatment by statistics.


Hospital stay and Improvement
Improved
Unimproved
Percentage
50.0
45.0
40.0
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
42.4
20.8
45.5
45.8
12.1
33.3
≤ 15 days
16 - 30 days
> 30 days
Hospitai Stay

TABLE NO 11

COMPARISON OF THE GROUPS ON

PREMORBID FUNCTIONING

Variables	Improvement	N	Mean	Std. Deviation	t-Value	p-Value
PSA Score	Improved	33	.282	.2038	1.654	0.104
	Unimproved	24	.379	.2395		

In the improved group the premorbid social adjustment mean score was 0.282 and in the unimproved group mean score was 0.379. The p value was 0.104. The difference between the two groups was not statistically significant.

TABLE NO 12

COMPARISON OF THE TWO GROUPS BY

MODE OF TREATMENT

Drugs Type used	Improvement					
	Improved		Unimproved		Total	
	N	%	N	%	N	%
Typical	5	15.2	19	79.2	24	42.2
Typical & Atypical	28	84.8	5	20.8	33	57.8
Total	33	100.0	24	100.0	57	100.0

Comparison of the two groups by mode of treatment

Chi-Square Test	Value	P-Value
Pearson Chi-Square	82.216	0.0001

In the improved group 28 patients (84.8%) were treated with both typical and atypical antipsychotic drugs. 5 patients (15.2%) with typical drugs. In unimproved groups 19 patients (79.2%) treated with typical drugs and only 5 patients (20.8%) were treated with typical as well as atypical antipsychotics. The p value is 0.0001 and hence the difference between two groups was statistically significant.

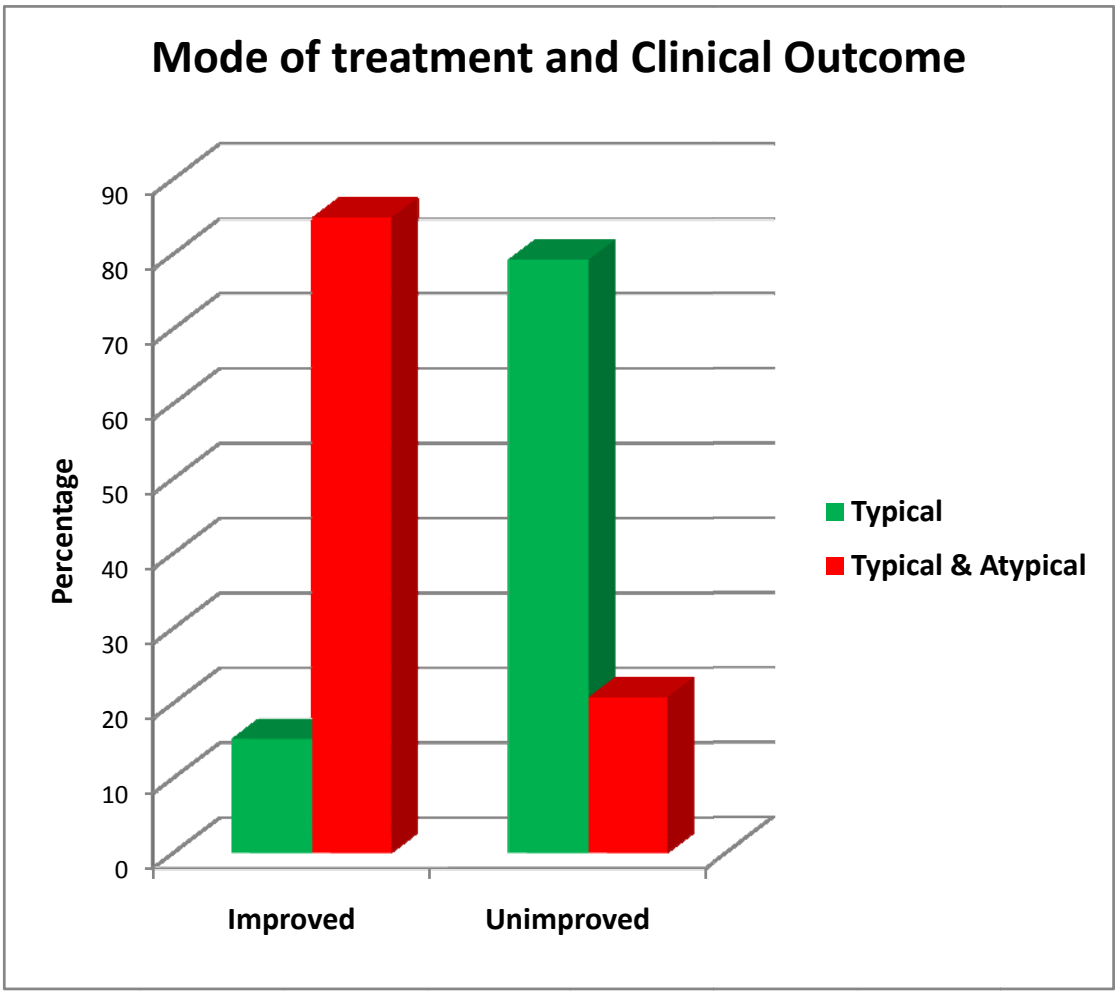

Mode of treatment and Clinical Outcome
Percentage
90
80
70
60
50
40
30
20
10
0
Improved
Unimproved
Typical
Typical & Atypical

TABLE NO 13

CORRELATION OF DUP WITH IMPROVEMENT AT 12 WEEKS

Duration of untreated psychosis	Clinical Outcome					
	Improved		Unimproved		Total	
	N	%	N	%	N	%
Below 1 year	12	36.4	0	0.0	12	21.1
1 - 2 years	16	48.5	2	8.3	18	31.6
> 2 years	5	15.2	22	91.7	27	47.4
Total	33	100.0	24	100.0	57	100.0

Correlation of DUP with improvement at 12 weeks

Chi-Square Test	Value	P-Value
Trend Chi-Square	28.284	<0.001

In improved group 12 patients (36.4%) showed less than 1 year of Duration of Untreated Psychosis. In unimproved group 27 patients (47.4%) showed more than 2 years of DUP. The p value is < 0.001 which is statistically significant.

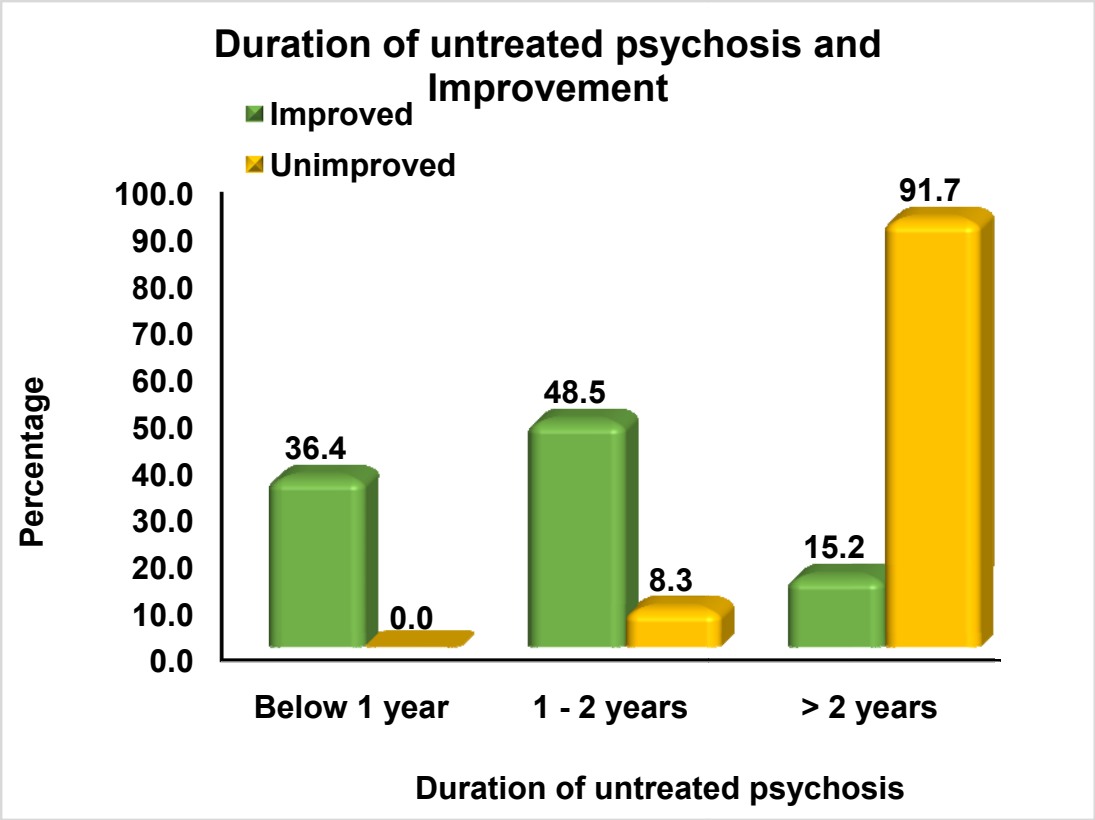

Duration of untreated psychosis and Improvement
Improved
Unimproved
Percentage
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
36.4
0.0
48.5
8.3
15.2
91.7
Below 1 year
1 - 2 years
> 2 years
Duration of untreated psychosis

TABLE NO 14

CORRELATION BETWEEN PREMORBID FUNCTIONING AND DUP

Test values		Duration of untreated psychosis
PSA Score	Pearson Correlation	0.366
	P-Value	0.005
	N	57

Poor premorbid functioning associated with longer DUP is statistically significant. The p value is <0.005. This is statistically significant.

TABLE NO 15

COMPARISON OF PREMORBID FUNCTIONING IN TWO GROUPS

Variables	Improvement	N	Mean	Std. Deviation	t-Value	P-Value
PSA Score	Improved	33	0.282	0.2038	1.654	0.104
	Unimproved	24	0.379	0.2395		

In improved group, the mean of PSA score was 0.282 and in unimproved group, mean of PSA is 0.239. It is not significant.

Independent samples t-test to compare mean values between Improve and unimproved cases

Variables	Improvement	N	Mean	Std. Deviation	t-Value	P-Value
Duration of untreated psychosis	Improved	33	1.6461	1.06216	5.631	<0.001
	Unimproved	24	4.9167	2.69729		
Age of onset of Illness	Improved	33	29.67	5.972	1.907	0.062
	Unimproved	24	26.79	5.090		
Duration of hospitalization (days)	Improved	33	24.70	15.357	2.419	0.021
	Unimproved	24	40.38	28.928		
Panss positive syndrome	Improved	33	19.00	7.365	0.382	0.704
	Unimproved	24	18.21	8.204		
Negative syndrome.	Improved	33	18.09	6.984	1.663	0.104
	Unimproved	24	22.00	9.860		
General psychopathology	Improved	33	33.30	6.405	0.729	0.472
	Unimproved	24	35.46	13.416		
CGI-S Score	Improved	33	4.33	.595	0.537	0.595
	Unimproved	24	4.46	1.021		
CGI-I Score	Improved	33	2.58	.502	13.418	<0.001
	Unimproved	24	4.21	.415		
PSA Score	Improved	33	.282	.2038		

We compared the Duration of untreated psychosis with improvement of psychosis by confounding other variables, like gender, socioeconomic status, duration of hospitalization, symptoms at the initial stages, general psychopathology and premorbid functioning. The DUP in our study showed a marked independent factor in predicting the clinical outcome statistically. The p value for DUP in this study is less than 0.001.

DISCUSSION

Studies state that a long duration of untreated psychosis associated with poor prognosis in schizophrenia.

Socio demographic variables and DUP:

The mean duration of untreated psychosis for whole sample is 3.02 years, which is longer than the DUP reported in studies done in Western countries, but mean DUP in this study is shorter when compared to some of the Indian studies (4 years in a study by Philip et al 11.64 years in a study by Padmavathi et al and more than 5 years by Tirupati et al). Among the whole sample 47.4% had a DUP greater than 2 years, which again confirms the finding that patient in developing countries come late to treatment (Isaac et al, Thara et al).

The role of socio demographic variables in determining the duration of untreated psychosis has given contrasting results across various studies. Studies have shown that males have a longer DUP than females, but we could not establish any such difference in gender to be associated with DUP. Numerous studies have not reported any relation of DUP with gender.

The finding of a significant positive correlation of DUP with the age at first presentation showed that the duration of untreated psychosis increases as the age at first presentation to treatment increases. The result

being similar to the finding of Padmavathi et al that never treated patients were older in age and ill for a longer duration and were more symptomatic and severely disabled. This finding is in contrary to other studies that have not found any association between age and DUP.

There is no significant correlation of duration of untreated psychosis with educational level, marital status and socioeconomic status at baseline assessment, a finding which is similar to most other studies. One study in India has reported that untreated patients were most often uneducated and divorced and such a finding is not found in our study. In our study we found no correlation between DUP and employment, a finding contrary to the report of Morgan et al that unemployment has a less strong effect on duration of untreated psychosis.

Some of the Indian studies have reported that a longer duration of untreated illness in schizophrenic patients was due to the larger extended/joint family, which was able to compensate and cope with the dysfunctional member, concluding that such family system seemed to be crucial factor related to delay in treatment. In our study, though 80.7% of the patients were in the joint family system, there was no significant correlation of family type with DUP. In west London first episode study of schizophrenia most of the patients were living alone or homeless. However this study carried out in a government institute has its

limitations regarding demographic variables like educational status, socioeconomic status and employment.

Clinical variables and DUP:

In our study there is significant association between undifferentiated schizophrenia of 10 patients (41.7%) with duration of untreated psychosis at baseline assessment. Only few studies have studied the relation of diagnostic subtype with DUP and have not found any significant association.

In our study premorbid functioning is found to have a positive correlation with duration of untreated psychosis, showing that poor premorbid functioning is associated with a longer DUP than those with a better premorbid functioning, this finding is similar the studies done by Verdoux et al and Mella et al where they have reported that poor premorbid functioning is associated with long DUP and poor outcome. Some of the studies have not shown any association between DUP and premorbid functioning.

The correlation of DUP with symptom severity at baseline in this study has found a significant negative correlation with positive symptoms, has significant but not with negative syndrome and general psychopathology. The finding is similar to studies that have found longer

DUP to be associated with higher levels of negative or deficit symptoms at first presentation (Perkins et al).

The negative correlation of DUP with positive symptom domain in the study implies that schizophrenic patients with positive symptoms seek treatment earlier and hence have a shorter duration of untreated psychosis. As Drake et al reported that longer DUP was associated higher positive symptoms at presentation which is present in our study. Some of the studies do not find any such association between DUP and baseline symptoms (Loebel et al, & Hass et al).

Total number of patients at 12 weeks assessment is 57 patients, and the follow up rate is considerably lower when compared to most other studies, both Indian and studies done in Western countries. The poor attrition rate could not be explained by any of the socio-demographic and clinical variables and the duration of untreated psychosis, finding similar to study done by Harris where they compared between those who completed follow up.

In the follow up assessment there is no significant difference between the improved and the unimproved group of patients on any of the socio-demographic variables such as education, socio-economic status, marital status, employment and family type. This is contrary to the studies that have shown that being married has a good outcome.

There is no significant association between the two groups by age, age at onset of illness which is contrary to the finding of Perkins et al that younger age at onset predicts a poor prognosis and is potential confounding factor of DUP and outcome.

DUP and out come at 12 weeks:

There is a statistically significant difference between the improved and the unimproved groups on the duration of untreated psychosis, as the mean DUP for the improved groups is and unimproved group of patients. This finding is similar to other studies that shorter DUP is associated with good outcome and treatment response than those with a longer DUP. In a study done by Philip et al, reported that patients with a short DUP have shown improvement at the end of 6 weeks following treatment. There have been contrasting reports that DUP has an influence on the outcome in the short term but not on the long term. Darke et al in his study concluded that DUP relationship to outcome is strongest in the initial months of psychosis and has implications for targeting early intervention.

The sub types of schizophrenia did not show any significant difference between the improved and unimproved groups though paranoid schizophrenia is the most common diagnosis in the sample.

In this study there is no difference among the two groups by family history suggestive of schizophrenia.

In this study the duration of hospitalization between the two groups was not significant as more than 1 month hospitalization in unimproved group is 33.3% and in improved groups it is 12.1 %. It is the same report observed by Hass et al that there is no significant difference in terms of duration of hospitalization between long and short DUP groups.

Treatment response:

The mode of treatment between the two groups is statistically significant. In improved group 28 patients (84.8 %) and in unimproved group (20.8%) were treated with both typical and atypical antipsychotics. This difference could not be explained by the fact that patients with short DUP would have had a better response to treatment as described by Perkins et al in his study. This result has to be interpreted with caution as the type of drugs, dosage, and adequacy of dose was not included in our study. Few studies differ as Barnes et al found that there was little evidence of any association between DUP and development of resistance to initial drug treatment.

In our study the premorbid social adjustment score is statistically significant between the improved and the unimproved groups, indicating that poor premorbid functioning is associated with poor improvement. This finding is similar to the reports of Verdoux et al that premorbid functioning is an important predictor of outcome. Again the premorbid social adjustment scale used in this study assesses premorbid functioning

in social and school activities, for which 45.5 % of sample is educated up to middle school and 6.1 % sample is uneducated in our study making it difficult to assess in these group of patients.

Confounding factors, DUP and outcome:

In order to find the relationship of confounding factors associated with DUP and outcome, an independent t-test was done, controlling for the confounding factors such as age at onset illness, severity of the symptoms domains of positive syndrome, negative syndrome, general psychopathology and premorbid functioning. The correlation found that DUP is statistically significant after controlling for the confounding factors ($p < 0.001$). This result shows that duration of Untreated Psychosis is an independent predictor of outcome.

As premorbid functioning have shown that it is not statistically correlated with improvement at 12 weeks ($p<0.104$). But premorbid functioning showed statistically significant correlation with DUP ($p<0.005$).

This finding is similar to studies that report premorbid functioning is not a strong predictor of outcome and the observed association between DUP and outcome was not explained by premorbid adjustment.

Thus in our study we found that DUP is an independent predictor of short term outcome of first episode schizophrenia.

SUMMARY AND CONCLUSION

The aim of the study is to find the social and clinical determinants of untreated psychosis, the influence of duration of untreated psychosis on short term outcome and relationship of premorbid functioning on duration of untreated psychosis and outcome at 12 weeks in sample of first episode drug naïve schizophrenia patients diagnosed according to the ICD-10. Strict inclusion and exclusion criteria were used to get a homogenous sample.

60 patients were selected for the study of which 57 were assessed at baseline with socio demographic profile, duration of untreated psychosis, PANSS and CGI-Severity for psychopathology, PSA scale to assess premorbid functioning. Details were obtained on admission; follow up assessment was done at 12 weeks. For treatment response 57 patients followed up and were categorized in to improved and unimproved as per CGI-I scale.

Reduction of PANSS symptoms, correlation of DUP with socio-demographic, and symptoms at baseline were done. Comparison between the improved and unimproved groups was done. Results were analyzed using chi-square test, t-test, and Pearson's correlation.

The study showed the following results

1. Significant positive correlation between duration of untreated psychosis and the age at first presentation.
2. Significant negative correlation between duration of untreated psychosis and positive symptoms at baseline.
3. Significant positive correlation between duration of untreated psychosis and premorbid functioning at base line.
4. Improved group patients had a better premorbid functioning than the unimproved group.
5. Improved group of patients had a short duration of untreated psychosis than the unimproved group.
6. Statistically significant difference between the improved and the unimproved groups by mode of treatment.
7. There is significant correlation of duration of untreated psychosis and premorbid functioning with improvement after confounding factors were controlled.
8. Thers is no significant difference between the improved and the unimproved groups in the negative symptoms at baseline.

The findings from this study suggest that a longer duration of untreated psychosis is associated with increased age at presentation, higher negative symptoms and poor premorbid functioning. The result

show that improved patients have a short duration of untreated psychosis and better premorbid functioning, the association is significant even after the confounding factors were controlled.

This finding concludes that duration of untreated psychosis is an independent predictor of outcome as stated in literature. So early intervention is necessary.

LIMITATIONS

1. While finding the onset of psychosis before admission to the hospital may have the usual recall bias by the patient and care giver.

2. As short term outcome was measured in this study the change in the symptoms after 12 weeks could be more a measure of treatment response, but not of social outcome and quality of life.

3. Variables related to duration of untreated psychosis such as pathways to care, mode of onset, substance use were not included.

4. Treatment details were not described in detail as it could have a significant influence on outcome.

5. The researcher was not completely blind to the patients at time of follow up assessment as literature says that there is a likely chance for bias in assessment.

IMPLICATIONS

Schizophrenia entails a progressive pathological course that is well established by the time the full blown psychopathology of psychosis appears. The correlation between DUP and clinical outcome gives hope that early intervention services that are effective in reducing the duration of the initial psychotic event may augment the likelihood of recovery from a first episode of schizophrenia and possibly decrease collective morbidity. Improving the symptoms of initial psychosis may benefit patients and their families, but it may also improve long-term prognosis by restricting progression of the disease and preserving a person's ability to respond to antipsychotic treatment.

In future, it will be essentially important to assess the effect of decline of the duration of untreated psychosis on initial negative symptom severity and negative symptom domain response to medical treatment. From a public health perspective, it is of chief importance to further study the relation between duration of untreated psychosis, premorbid characteristics, outcome in large sample sizes and in studies aimed at correlating the impact of early case finding and treatment of schizophrenia.

FUTURE DIRECTIONS

Trials, that improve our knowledge of understanding of the possible mechanism for correlation between DUP and clinical outcome should be done in the future which may give more critical information about the neuropathology of first episode of schizophrenia. The neuro-developmental and possible progressive features of brain changes should be observed in first episode of schizophrenia in the future.

The proof for clinical worsening after a long period of initially untreated first episode psychosis, manifested through the onset of secondary resistance to treatment with antipsychotics and progressive functional impairments, suggests that part of the clinical worsening characters of schizophrenia is mediated by a progressive patho-physiological process.

Studying schizophrenia over the lifespan including chronic, first episode, early and late onset, and prodromal patients and also subgroups of patients who respong and who do not respond well to medication by finding the which brain changes can be detected early in the course of the illness an d how, this changes progress and whether or not there are difference in brain appearance between clinical subtypes of schizophrenia.

Relationship between gene and brain development and illness onset and progression need to be investigated. Further studies that involve and combine multiple in vivo methodologies such as structural MRI, Mangnetization transfer ration (MTR), DTI (Diffusion Tensor Imaging) on one hand, and functional MRI, PET-Positron Emission Tomography and spectroscopy on other hand are already emerging. This should replace single modality approaches within the next few years. This change from single to multimodal imaging in the same patient will increase the understanding of the relationship between functional and structural brain abnormalities in schizophrenia and lay the foundation for linking such findings to signature cognitive impairments and susceptibility genes. There will be likely more studies of treatment efficacy and more attention paid to the critical period following first episode, where progressive changes in the brain are most evident.

At the end of this study we suggest that the future studies should include other factors such as recognition of illness, access to and availability of care for schizophrenia, social stigma, associated peri-natal complications and neurological soft signs.

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APPENDIX 1

Semi structured Proforma

Name

Age

Sex

Eduction-uneducted/primary/middle/high school/graduate

Occupation-employed/un employed

Socio economic status-low/middle/high

Marital status-married/separated/divorced/widow/un married

Type of family-nuclear/joint

Family history-yes/no

Age at onset-

Diagnosis-paranoid/hebephrenic/catatonic/undifferentiated/simple

Duration of untreated psychosis

Duration of hospitalization

Anti psychotic treatment-

APPENDIX 2

PANSS

Positive Scale (Score 0 – 7)

P1Delusions

P2Conceptual disorganization

P3Hallucinatory behavior

P4Excitement

P5Grandiosity

P6Suspiciousness

P7Hostility

Scale total-49

Negative Scale (Score 0 – 7)

N1Blunted affect

N2Emotional withdrawal

N3Poor rapport

N4Passive-apathetic social withdrawal

N5Difficulty in abstract thinking

N6Lack of spontaneity & flow of conversation

N7Stereotyped thinking

Scale total-49

General Psychopathology Scale (Score 0 – 7)

G1Somatic concern

G2Anxiety

G3Guilt feelings

G4Tension

G5Mannerisms & posturing

G6Depression

G7Motor retardation

G8UncooperatJveness

G9Unusual thought content

G10Disorientation

G11Poor attention

G12Lack of judgment & insight

G13Disturbance of volition

G14Poor impulse control

G15Preoccupation

G16Active social avoidance

Scale total-210

APPENDIX - 3

Clinical global impression scale

1. Severity of illnes

0 = Not assessed 4 = Moderately ill

1 = Normal, not at all ill 5 = Markedly ill

2 = Borderline mentally ill 6 = Severely ill

3 = Mildly ill 7 = Among the most extremely ill patients

2. Global improvement: Rate total improvement whether or not, in your judgement, it is due entirely to drug treatment.

Compared to his condition at admission to the project, how much has he changed?

0 = Not assessed 4 = No change

1 = Very much improved 5 = Minimally worse

2 = Much improved 6 = Much worse

3 = Minimally improved 7 = Very much worse

APPENDIX - 4

Premorbid social adjustment scale

Childhood (up through age 11)

1. Sociability and withdrawal

0 - Not withdrawn, actively and frequently seeks out social contacts

2 - Mild withdrawal, enjoys socialization when involved, occasionally seeks opportunities to socialize

4 - Moderately withdrawn, given to daydreaming and excessive fantasy, may passively allow self to be drawn into contact with others, but does not seek it

6 - Unrelated to others, withdrawn and isolated, avoids contacts

2. Peer relationships

0 - Many friends (*more than 5*), close relationships ("*best friends" or people you could confide in*) with several

1 - *2–5 friends*

2 - Close relationships with a few friends (1 or 2), casual friendships with others

3 - *Only casual friends*

4 - Deviant (*unusual*) friendship patterns: friendly with children younger or older only, or relatives only, or casual relationships only

6 - Social isolate, no friends, not even superficial relationships

3. Scholastic performance (*as compared with all other students that age in the general population [i.e., a student doing very well in a special needs school would rate no higher than a 4]*)

0 - Excellent student (*straight A's – likely to attend a post-secondary institution*)

1 - *A's and B's* (*likely to pursue post-secondary studies*)

2 - Good student (*B's – post-secondary*)

3 - *Average student* (*B's and C's*)

4 - Fair student (*C's*)

5 - *D's – failing some classes*

6 - Failing all classes

4. Adaptation to school

0 - Good adaptation, enjoys school, no or rare discipline problems, has friends at school, likes most teachers

1 - *Likes school, few discipline problems*

2 - Fair adaptation, occasional discipline problems, not very interested in school, but no truancy or rare. Has friends in school, but does not often take part in extracurricular activities

3 - *Sometimes truant*

4 - Poor adaptation, dislikes school, frequent truancy, frequent discipline problem (*may have been suspended*)

5 - *Expelled from school*

6 - Refuses to have anything to do with school — delinquency or vandalism directed against school

Early adolescence (12–15 years of age)

1. Sociability and withdrawal

0 - Not withdrawn

2 - Mild withdrawal, enjoys socialization when involved, occasionally seeks opportunities to socialize

4 - Moderately withdrawn, given to daydreaming and excessive fantasy, may passively allow self to be drawn into contact with others, but does not seek it

6 - Unrelated to others, withdrawn and isolated, avoids contact

2. Peer relationships

0 - Many friends (*more than 5*), close relationships (“*best friends” or people you could confide in*) with several

1 - *2–5 friends*

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3. Scholastic performance (*as compared with all other students that age in the general population [i.e., a student doing very well in a special needs school would rate no higher than a 4]*)

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3 - *Sometimes truant*

4 - Poor adaptation, dislikes school, frequent truancy, frequent

discipline problem (*may have been suspended*)

5 - *Expelled from school*

6 - Refuses to have anything to do with school — delinquency or vandalism directed against school

5. Social-sexual aspects of life during early adolescence

0 - Started dating, showed a “healthy interest” in the opposite sex, may have gone “steady,” may include some sexual activity

1 - Attachment and interest in others, may be same-sex attachments, may be a member of a group, interested in the opposite sex, although may not have close, emotional relationship with someone of the opposite sex, “crushes” and flirtations

2 - Consistent deep interest in same-sex attachments with restricted or no interest in the opposite sex

3 - Casual same-sex attachments with inadequate attempts at relationships with the opposite sex. Casual contacts with both sexes

4 - Casual contacts with the same sex, no interest in the opposite sex

5 - A loner, no or rare contacts with either boys or girls

6 - Antisocial, avoids and avoided by peers (differs from above in that an active avoidance of others rather than a passive withdrawal is implied)

Late adolescence (16–18 years of age)

1. Sociability and withdrawal

0 - Not withdrawn

2 - Mild withdrawal, enjoys socialization when involved, occasionally seeks opportunities to socialize

4 - Moderately withdrawn, given to daydreaming and excessive fantasy, may passively allow self to be drawn into contact with others, but does not seek it

6 - Unrelated to others, withdrawn and isolated, avoids contact

2. Peer relationships

0 - Many friends (*more than 5*), close relationships (*"best friends" orpeople you could confide in*) with several

1 - *2–5 friends*

2 - Close relationships with a few friends (1 or 2), casual friendships with others

3 - *Only casual friends*

4 - Deviant (*unusual*) friendship patterns: friendly with children younger or older only, or relatives only, or casual relationships only

6 - Social isolate, no friends, not even superficial relationships

3. Scholastic performance (*as compared with all other students that age in the general population [i.e., a student doing very well in a special needs school would rate no higher than a 4])*

0 - Excellent student (*straight A's – likely to attend a post-secondary institution*)

1 - *A's and B's* (*likely to pursue post-secondary studies*)

2 - Good student (*B's – post-secondary*)

3 - *Average student* (*B's and C's*)

4 - Fair student (*C's*)

5 - *D's – failing some classes*

6 - Failing all classes

4. Adaptation to school

0 - Good adaptation, enjoys school, no or rare discipline problems, has friends at school, likes most teachers

1 - *Likes school, few discipline problems*

2 - Fair adaptation, occasional discipline problems, not very interested in school, but no truancy or rare. Has friends in school, but does not often take part in extracurricular activities

3 - *Sometimes truant*

4 - Poor adaptation, dislikes school, frequent truancy, frequent discipline problem (*may have been suspended*)

5 - *Expelled from school*

6 - Refuses to have anything to do with school — delinquency or vandalism directed against school

5. Social-sexual aspects of life during early adolescence

0 - Always showed a “healthy interest” in the opposite sex, dating, has gone “steady,” has engaged in some sexual activity (not necessarily intercourse)

1 - Dated regularly. Had only one friend of the opposite sex with whom the subject went “steady” for a long time. (Includes sexual aspects of a relationship, although not necessarily intercourse; implies a twosome, pairing off into couples as distinguished from below)

2 - Always mixed closely with boys and girls. (Involves membership in a crowd, interest in and attachment to others, no couples)

3 - Consistent deep interest in same-sex attachments with restricted or no interest in the opposite sex

4 - Casual same-sex attachments with inadequate attempts at adjustment to going out with the opposite sex. Casual contacts with both sexes

5 - Casual contacts with the same sex, with a lack of interest in the opposite sex. Occasional contacts with the opposite sex

6 - No desire to be with boys and girls, never went out with the opposite sex

Adulthood (age 19 and above)

1. Sociability and withdrawal

0 - Not withdrawn, actively and frequently seeks out social contact

2 - Mild withdrawal, enjoys socialization when involved, occasionally seeks opportunities to socialize

4 - Moderately withdrawn, given to daydreaming and excessive fantasy, may passively allow self to be drawn into contact with others, but does not seek it

6 - Unrelated to others, withdrawn and isolated, avoids contact

2. Peer relationships

0 - Many friends (*more than 5*), close relationships (*"best friends" or people you could confide in*) with several

1 - *2–5 friends*

2 - Close relationships with a few friends (1 or 2), casual friendships with others

3 - *Only casual friends*

4 - Deviant (*unusual*) friendship patterns: friendly with children younger or older only, or relatives only, or casual relationships only

6 - Social isolate, no friends, not even superficial relationships

3. Aspects of adult social-sexual life

A. Married presently or formerly

0 - Married, only one marriage (or remarried as a result of death of spouse), living as a unit, adequate sexual relations

1 - Currently married with a history of low sexual drive, periods of

difficult sexual relations, or extramarital affair

1 - Married more than one time, currently remarried. Adequate sexual relations during at least one marriage

2 - Married, or divorced and remarried, with chronically inadequate sex life

2 - Married and apparently permanently separated or divorced without remarriage, but maintained a home in one marriage for at least 3 years

3 - Same as above, but divorce occurred over 3 years ago and while married, maintained a home for less than 3 years

B. Never married, over 30 years of age

2 - Has been engaged one or more times or has had a long-term relationship (at least 2 years) involving heterosexual or homosexual relations, or apparent evidence of a love affair with one person, but unable to achieve a long-term commitment such as marriage

3 - Long-term heterosexual or homosexual relationship lasting over 6 months, but less than 2 years

4 - Brief or short-term dating experiences (heterosexual or homosexual) with one or more partners, but no long-lasting sexual experience with a single partner

5 - Sexual and/or social relationships rare or infrequent

6 - Minimal sexual or social interest in either men or women, isolated

C. Never married, age 19–29 years

0 - Has had at least one long-term love affair (minimum 6 months) or engagement, even though religious or other prohibitions or inhibitions may have prevented actual sexual union. May have lived together

1 - Has dated actively, had several “boyfriends” or “girlfriends.” Some relationships have lasted a few months, but no long-term relationships. Relationships may have been serious but a long-term commitment such as marriage was not understood to be an eventuality

3 - Brief or short-term dating experiences or affairs with one or more partners, but no long-lasting sexual experience with a single partner

4 - Casual sexual or social relationships with persons of either sex with no deep emotional bonds

5 - Sexual and/or social relationships rare or infrequent

6 - Minimal sexual or social interest in either men or women, isolated

INFORMATION TO PARTICIPANTS

Title:
- Influence of duration of untreated psychosis on the short term outcome in first episode schizophrenia

Principal Investigator: Dr.K.BHARATHI,
Third Year, MD Psychiatry Post Graduate,
Madras Medical College
Co-Investigator(if any):

Name of Participant:

Site : IMH, MMC, Chennai

You are invited to take part in this research. The information in this document is meant to help you decide whether or not to take part. Please feel free to ask if you have any queries or concerns.

What is the purpose of research?

- Schizoprenia is a chronic disabling disorder for most affected individuals.vulnerablity to schizophrenia is releated to genetic and environmental factors that influence early brain development.About prognosis most recent studies suggest that early intervention can improve outcome.Relationship of duration of untreated psychosis and outcome may indicate a neurodegenerative process and so have important implication for understanding the pathophysiology of schizophrenia.Understanding cause and consequence of untreated psychosis is important because duration of psychosis before intiation of treatment is potentially modifiable prognostic factors,understanding relation to outcome could lead to improved therapeutic strategies and public health intiatives.

The study design
You will be interviewed by the bedside while you are admitted in our hospital.

Study Procedures
The study involves evaluation of time of emeregence of psychotic symptom ,severity of symptoms and clinical and social outcome assessment for which we will be interviewing you with various questionnaires. You will be required to spare roughly half an hour for a one-time interview during your stay in the hospital.

Possible benefits to you - If you are found to have schizoprenia first episode never treated you will be treated in imh and have a followup for 12 weeks

Possible benefits to other people
The results of the research may provide benefits to the society in terms of advancement of medical knowledge and/or therapeutic benefit to future patients.
Confidentiality of the information obtained from you
You have the right to confidentiality regarding the privacy of your medical information (personal details, results of physical examinations, investigations, and your medical history). By signing this document, you will be allowing the research team investigators, other study personnel and the Institutional Ethics Committee, to view your data, if required.

The information from this study, if published in scientific journals or presented at scientific meetings, will not reveal your identity.

How will your decision to not participate in the study affect you?
Your decision not to participate in this research study will not affect your medical care or your relationship with the investigator or the institution. You will be taken care of and you will not lose any benefits to which you are entitled.
Can you decide to stop participating in the study once you start?
The participation in this research is purely voluntary and you have the right to withdraw from this study at any time during the course of the study without giving any reasons. However, it is advisable that you talk to the research team prior to stopping the treatment/discontinuing of procedures etc.

Signature of Investigator Signature of Participant

date date

ஆராய்ச்சி தகவல் தாள்

தலைப்பு: சிகிச்சை அளிக்க கால தாமதமாகும் மனசிதைவு நோயாளிகளுக்கு நோயின் முன்னேற்றம் எவ்வாறு இருக்கும் என்பதை பற்றிய ஆய்வு

ஆராய்ச்சி செய்பவரின் பெயர்: கு. பாரதி

பங்குகொள்வரின் பெயர்:

மருத்துவ நிலையம்: அரசு மனநல காப்பகம், சென்னை

சிகிச்சை அளிக்க கால தாமதமாகும் மனசிதைவு நோயாளிகளுக்கு நோயின் முன்னேற்றம் எவ்வாறு இருக்கும் என்பதை பற்றிய ஆய்வு இதில் தங்களுக்கு நோயின் தன்மை, நோய்க்கு முன்னாள் நீங்கள் எவ்வாறு இருந்தீர்கள் என்பதைப் பற்றி உங்களிடமும் உங்கள் உறவினரிடமும் கேள்விகள் கேட்கப்படும்.

முடிவுகளை அல்லது கருத்துக்களை வெளியிடும்போதோ அல்லது ஆராய்ச்சியின் போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டோம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆய்வின் முடிவுகளை ஆராய்ச்சியின்போது அல்லது ஆராய்ச்சியின் முடிவின் போது தங்களுக்கு அறிவிக்கப்படும் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக் கொள்கிறோம்.

ஆராய்ச்சியாளரின் கையொப்பம் **பங்கேற்பாளர் கையொப்பம்**

நாள்:_____ நாள்:_____

பாதுகாவலர் கையொப்பம்

நாள்:_____

Informed consent form

Title of the study - Influence of duration of untreated psychosis on the short term outcome of first episode schizophrenia

Name of the participant: _____

Name of the Principal/Co-Investigator: DR. K.BHARATHI

Name of the Institution: IMH, MMC

Name and address of the sponsor / agency(ies), if any: _____

I,_____(name of participant), have read the information in this form (or it has been read to me). I was free to ask any questions and they have been answered. I am over 18 years of age and, exercising my free power of choice, hereby give my consent to be included as a participant in the study about the - Influence of duration of untreated psychosis on the short term outcome of first episode schizophrenia

(1) I have read and understood this consent form and the information provided to me.

(2) I have had the consent document explained to me.

(3) I have been explained about the nature of the study.

(4) I have been explained about my rights and responsibilities by the investigator.

(5) I have informed the investigator of all the treatments I am taking or have taken in the past, including any native (alternative) treatments.

(6) I am aware of the fact that I can opt out of the study at any time without having to give any reason and this will not affect my future treatment in the hospital.

(7) I hereby give permission to the investigators to release the information obtained from me as result of participation in this study to the regulatory authorities, Government agencies, and ethics committee. I understand that they may inspect my original records.

(8) I understand that my identity will be kept confidential if my data are publicly presented.

(9) I have had my questions answered to my satisfaction.

(10) I consent voluntarily to participate as a participant in the research study.

I am aware, that if I have any questions during this study, I should contact the investigators. By signing this consent from, I attest that the information given in this document has been clearly explained to me and understood by me. I will be given a copy of this consent document.

For adult participants

Name and signature / thumb impression of the participant (or legal representative if participant Is incompetent):

(Name) _____(Signature)_____ Date: _____

Name and signature of impartial witness (required for illiterate patients):

(Name) _____ (Signature)_____ Date:_____

Address and contact number of the impartial witness: _____

Name and signature of the Investigator or his representative obtaining consent:

(Name) _____ (Signature)_____ (Date)_____

ஆராய்ச்சி ஒப்புதல் படிவம்

ஆராய்ச்சியின் தலைப்பு- சிகிச்சை அளிக்க காலதாமதமாகும் மனசிதைவு நோயாளிகளுக்கு நோயின் முன்னேற்றம் எவ்வாறு இருக்கும் என்பதை பற்றிய ஆய்வு

பங்குகொள்வரின் பெயர்:

ஆராய்ச்சி செய்பவரின் பெயர்: மரு. **கு. பாரதி**

மருத்துவ நிலையம்: அரசு மனநல காப்பகம், சென்னை

_____எனும் நான் எனக்கு கொடுக்கப்பட்ட தகவல் தாளினை படித்து புரிந்துகொண்டேன். நான் 18 வயதை கடந்திருப்பதால் என்னுடைய சுய நினைவுடனும் மற்றும் முழு சுதந்திரத்துடனும் இந்த ஆராய்ச்சியில் என்னைச் சேர்த்துக்கொள்ள சம்மதிக்கிறேன்.

நான் எனக்கு கொடுக்கப்பட்ட தகவல் தாளினை படித்து புரிந்துகொண்டேன்.

எனக்கு இந்த ஆராய்ச்சியின் ஒப்புதல் படிவம் விளக்கப்பட்டது.

எனக்கு இந்த ஆராய்ச்சியின் நோக்கமும், விவரங்களும் விளக்கப்பட்டது.

எனக்கு என்னுடைய உரிமைகளை பற்றி விளக்கப்பட்டது.

நான் இதுவரை எடுத்துக்கொண்ட அணைத்து மருத்துவ முறைகளைப் பற்றி தெரிவித்திருக்கிறேன்.

இந்த ஆராய்ச்சியில் இருந்து நான் எந்நேரமும் பின் வாங்கலாம் என்பதையும் அதனால் எந்த பாதிப்பும் எற்படாது என்பதையும் நான் புரிந்துகொண்டேன்.

என்னை பற்றிய எந்த தகவல்களும் அடையாளமும் வெளியிடபட மாட்டாது என்பதை நான் புரிந்துகொண்டேன்.

என்னுடைய முழு சுதந்திரத்துடனும் இந்த ஆராய்ச்சியில் என்னைச் சேர்த்துக்கொள்ள சம்மதிக்கிறேன்.

பங்கேற்பாளர் பெயர் மற்றும் கையொப்பம்:_____&_____

நாள்:_____

பாதுகாவலர் பெயர் மற்றும் கையொப்பம்: _____&_____

நாள்:_____

ஆராய்ச்சியாளரின் பெயர் மற்றும் கையொப்பம்:_____&_____ நாள்:_____

S.NO	Age	Sex	eduction	occupation	socioeconomic status	type of family	marital status	religion	family history of schizoprenia	duration of untreated psychosis	Age of onset of Illness	type of schizoprenia	Drugs used	duration of hospitilisation	panss positive syndrome	negative syndrome.	genaral psychopathology	CGI-S	CGI-I	PMS A
1	32	f	middle	unemployed	low	nuclear	married	hindu	no	2yr	30	paranoid	T.HPL,T.RISPERIDONE	1 MONTH	17	10	27	5	3	O.5
2	37	m	diploma	employed	low	joint	single	hindu	no	2 years	35	undifferetiaed	T.HPL,T.RISPERIDONE	2 MONTH	10	18	33	5	3	0.6
3	36	f	middle	unemployed	low	joint	single	hindu	no	6 yrs	30	undifferentied	t.HPL,T.RISPERIDONE	3 MONTH	14	28	37	5	4	0.6
4	42	m	primary	unemployed	low	joint	single	hindu	no	10yrs	32	undifferentied	t.HPL,T.olanzapine	3 MONTH	11	23	32	5	4	0.4
5	37	m	secondary	unemployed	low	nuclear	single	islam	yes	4 month	36	paranoid	t.risperidone	15 DAYS	34	23	45	5	2	0.3
6	35	m	middle	employed	middle	nuclear	married	hindu	no	3 yrs	32	paranoid	t.HPL,T.olanzapine	1 MONTH	30	19	33	6	4	0.4
7	32	f	primary	unemployed	low	nuclear	married	hindu	no	5yrs	27	paranoid	t.HPL,T.olanzapine	3 MONTHS	30	9	15	4	5	0.5
8	32	f	uneducated	unemployed	low	nuclear	single		no	2yrs	30	paranoid	T.HPL,T.RISPERIDONE	15 days	32	10	16	5	3	0.5
9	38	m	uneducated	employed	low	nuclear	married	hin	no	2 yrs	36	undifferentied	typical,atypical	I MONTH	12	23	32	4	2	0.3
10	23	f	secondary	unemployed	low	nuclear	married		yes	6years	17	hebeprenic	t.hpl,t.cpz,t.risperidone	20 days	9	32	54	5	5	0.6
11	38	f	middle	unemployed	low	nuclear	married		yes	3yrs	35	paranoid	t.hpl,t.cpz,t.risperidone	1 month	19	18	38	4	3	0.6
12	26	f	primary	unemployed	low	nuclear	single		no	1.5 yrs	24	undiffrentiated	t.HPL,T.olanzapine	1month	9	27	32	4	3	0.5
13	33	m	diploma	unemployed	low	nuclear	single		no	3months	32	paranoid	t.hpl	15 days	20	7	32	4	2	0.3
14	23	m	middle	employed	middle	nuclear	single		yes	7month	22	paanoid	t.olanzepine	20 days	20	22	32	4	2	0.3
15	40	m	degree	unemployed	low	joint	married		yes	5yrs	35	paranoid	T.HPL,T.RISPERIDONE	2.4 months	15	19	30	3	4	0.6

16	26	m	primary	employed	low	nuclear	married/separted		no	3yrs	23	undifferentied	t.hpl,t.cpz,	20 days	20	16	30	3	4	0.5
17	37	m	secondary	employed	low	nuclear	married		no	10yrs	27	paranoid	t.hpl,t.cpz,t.risperidone	2.5 months	14	11	33	3	4	0.2
18	31	m	middle	employed	low	nuclear	married		no	6months	30	paranoid	t.olanzepine	10 days	21	20	35	4	2	0.7
19	19	m	secondary	employed	middle	nuclear	single		yes	1yr	18	paranoid	t.risperidone	20 days	20	7	32	3	2	0.3
20	38	m	middle	employed	middle	joint	single		no	6 months	37	catatonic	t.HPL,T.olanzapine	1 MONTH	24	16	36	5	2	0.2
21	26	m	middle	unemployed	low	nuclear	single		yes	2.5 yrs	23	undiffreentiated	t.risperidone	20 days	11	31	32	4	4	0.2
22	28	m	primary	unemployed	low	nuclear	single		no	2yrs	26	paranoid	t.risperidone	1 MONTH	14	21	30	4	3	0.1
23	25	m	secondary	employed	middle	nuclear	single		no	3yrs	22	catatonic	T.HPL,T.RISPERIDONE	2 month	18	39	68	6	5	0.6
24	42	m	middle	employed	low	joint	married		no	2yrs	38	undifferentied	t.risperidone	10 days	9	29	42	5	3	0.2
25	28	m	middle	unemployed	low	nuclear	single		yes	2yrs	26	paranoid	t.risperidone	10 days	25	16	35	5	2	0.2
26	26	m	middle	employed	middle	nuclear	married		no	2yrs	24	paranoid	t.hpl,t.pz,t.risperidone	1 MONTH	24	16	34	5	2	0.2
27	36	m	middle	unemployed	low	nuclear	single		no	6yrs	30	catatonic	thpl,t.olanzepine	3 months	14	7	36	4	4	0.8
28	28	m	secondary	employed	low	nuclear	married		yes	3yrs	25	paranoid	t.hpl	10 days	15	27	38	4	3	0.1
29	27	m	middle	employed	low	nuclear	single		no	3yrs	24	paranoid	t.hpl	10 days	30	11	30	4	4	0.2
30	32	f	middle	unemployed	low	nuclear	married	hindu	no	2yr	30	paranoid	t.hpl	20 days	17	10	27	5	3	0.4
31	37	m	diploma	employed	middle	joint	single	hindu	no	2 years	35	undifferetiaed	T.HPL,T.RISPERIDONE	1 MONTH	10	18	33	5	3	0.8
32	36	f	middle	employed	middle	joint	single	hindu	no	6 yrs	30	undifferentied	T.HPL,T.RISPERIDONE	1MONTH	14	28	37	5	4	0.2
33	42	m	diploma	employed	low	joint	single	hindu	no	10yrs	32	undifferentied	t.risperidone	10 days	11	23	32	5	4	0.8
34	37	m	secondary	unemployed	low	nuclear	single	islam	yes	4 month	36	paranoid	t.olanzepine	15 days	34	23	45	5	2	0.1
35	35	m	middle	employed	low	nuclear	married	hindu	no	3 yrs	32	paranoid	t hpl,t.cpz	20 days	30	19	33	6	4	0.1
36	32	f	middle	unemployed	low	nuclear	married	hindu	yes	5yrs	27	paranoid	t.hpl,t.cpz	20 days	30	9	16	3	3	0.1

37	32	f	uneducated	employed	low	nuclear	single		no	2yrs	30	paranoid	t.risperidone	14 days	30	10	16	3	4	0.1
38	38	m	primary	employed	low	nuclear	married	hin	no	2 yrs	36	undifferentied	t.HPL,T.olanzapine	1 month	12	23	32	4	3	0.1
39	23	f	uneducated	employed	middle	nuclear	married		yes	6years	17	hebeprenic	thpl,t.olanzepine	2 month	9	32	54	5	5	0.5
40	38	f	middle	unemployed	low	nuclear	married		yes	3yrs	35	paranoid	t.hpl,t.cpz	15 days	19	18	38	4	3	0.1
41	26	f	middle	unemployed	low	nuclear	single		no	1.5 yrs	24	undiffrentiated	t.olanzepine	10 days	9	27	32	4	3	0.3
42	33	m	diploma	unemployed	middle	nuclear	single		no	3months	32	paranoid	t.HPL,T.olanzapine	1month	20	7	32	4	2	0.3
43	23	m	primary	unemployed	low	nuclear	single		no	7month	22	paranoid	t.risperidone	15 days	20	22	32	4	2	0.1
44	40	m	degree	employed	low	nuclear	married		no	5yrs	35	undifferentied	t.hpl,t.rISPERIDONE	1 month	15	19	29	3	4	0.6
45	26	m	primary	employed	low	nuclear	married/sep		no	3yrs	23	undifferentied	t.risperidone	15 days	9	30	24	5	4	0.1
46	37	m	secondary	employed	low	nuclear	married		yes	10yrs	27	catatonic	T.HPL,T.RISPERIDONE	1 month	14	30	24	4	4	0.6
47	31	m	secondary	employed	low	joint	married		no	6months	30	paranoid	thpl,t.olanzepine	2 month	21	20	35	4	2	0.1
48	2o	m	12	unemployed	high	nuclear	single		no	1yr	18	paranoid	t.hpl	10 days	30	10	36	4	3	0.5
49	38	m	middle	employed	low	nuclear	single		no	6 months	37	paranoid	t.olanzepine	15 days	24	16	36	5	2	0.1
50	26	m	degree	employed	low	nuclear	single		no	2.5 yrs	23	undiffreentiated	t.hpl,t.cpz,t.risperidone	1 month	11	31	32	4	4	0.2
51	28	m	middle	unemployed	low	nuclear	single		yes	2yrs	26	paranoid	t.olanzepine	10 days	14	21	30	4	3	0
52	25	m	secondary	unemployed	low	nuclear	single		no	3yrs	22	undifferentied	t.risperidone	15 days	18	39	68	6	5	0.1
53	40	m	secondary	unemployed	low	joint	married		no	2yrs	38	undifferentied	t.HPL,T.olanzapine	2 MONTH	9	29	42	5	3	0.1
54	28	m	middle	unemployed	low	nuclear	single		no	2yrs	26	paranoid	t.HPL,T.olanzapine	1 month	30	11	42	5	4	0.1
55	26	m	middle	unemployed	low	nuclear	married		no	2yrs	24	paranoid	t.hpl,t.rISPERIDONE	2 months	18	7	26	4	3	0.2
56	36	m	primary	employed	low	nuclear	married		no	3yrs	25	paranoid	t.olanzepine	20 days	15	27	38	4	3	0.1

57	28	m	middle	unemployed	low	nuclear	single		no	3yrs	24	paranoid	t.HPL,T.olanzapine	20 days	30	11	30	4	4	0.1